

## COVID-19 Resource Desk

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### New Research

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

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

### Clinical Syndrome

- 1. COVID-19 as the cause of thrombosis: recognising COVID-19 infection in apparently asymptomatic patients.** Varner KB, Cox EJ. [*Providence authors*]. *BMJ Case Rep*. 2021 Jan 7;14(1):e241027. doi: 10.1136/bcr-2020-241027. <https://casereports.bmj.com/content/bmjcr/14/1/e241027.full.pdf>  
Findings: COVID-19 has serious thrombotic complications in critically ill patients; however, thrombus is not a typical presenting symptom. This case report describes a patient with no respiratory symptoms who presented to the emergency department with abdominal pain. The pain was attributed to renal thrombosis, but the patient was found to have no risk factors for thrombotic disease and subsequent hypercoagulable work-up was unremarkable. Pulmonary manifestations of COVID-19 infection were detected incidentally on the abdominal CT scan and confirmed via PCR test. The patient was isolated and went on to develop mild respiratory failure secondary to COVID-19 infection. This case suggests that unexplained thrombus in otherwise asymptomatic patients can be a direct result of COVID-19 infection, and serves as a call to action for emergency department clinicians to treat unexplained thrombotic events as evidence of COVID-19.
- 2. Venous thromboembolism and major bleeding in patients with COVID-19: A nationwide population-based cohort study.** Dalager-Pedersen M, Lund LC, Mariager T, et al. *Clin Infect Dis*. 2021 Jan 5:ciab003. doi: 10.1093/cid/ciab003. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab003/6064643>  
Findings: Using nationwide population-based registries, 30-day risks of VTE and major bleeding in SARS-CoV-2 positive patients were compared with those of SARS-CoV-2 test-negative patients and with an external cohort of influenza patients. The overall 30-day risk of VTE was 0.4% (40/9,460) among SARS-CoV-2 patients (16% hospitalized), 0.3% (649/226,510) among SARS-CoV-2 negative subjects (12% hospitalized), and 1.0% (158/16,281) among influenza patients (59% hospitalized). VTE risks were higher and comparable in hospitalized SARS-CoV-2 positive (1.5%), SARS-CoV-2 negative (1.8%), and influenza patients (1.5%). Diagnosis of major bleeding was registered in 0.5% (47/9,460) of all SARS-CoV-2 positive individuals and in 2.3% of those hospitalized. Medical record review of 582 hospitalized SARS-CoV-2 patients observed

VTE in 4% (19/450) and major bleeding in 0.4% (2/450) of ward patients, of whom 31% received thromboprophylaxis. Among intensive care patients (100% received thromboprophylaxis), risks were 7% (9/132) for VTE and 11% (15/132) for major bleeding. Among people with SARS-CoV-2 infection in a population-based setting, VTE risks were low to moderate and were not substantially increased compared with SARS-CoV-2 test-negative and influenza patients. Risk of severe bleeding was low for ward patients, but mirrored VTE risk in the intensive care setting.

3. **The chronic kidney disease and acute kidney injury involvement in COVID-19 pandemic: A systematic review and meta-analysis.** Liu YF, Zhang Z, Pan XL, et al. *PLoS One*. 2021 Jan 5;16(1):e0244779. doi: 10.1371/journal.pone.0244779.

<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0244779>

Findings: Thirty-six trials were included in this systematic review with a total of 6395 COVID-19 patients. The overall effects indicated that preexisting CKD, complication of AKI, serum creatinine, abnormal serum creatinine, blood urea nitrogen, abnormal blood urea nitrogen, received continuous renal replacement therapy (CRRT) were significantly increased in severe group than that in nonsevere group. Additionally, the complication of AKI and blood urea nitrogen were remarkably elevated in the critical group than that in the severe group. CKD and AKI are susceptible to occur in patients with severe COVID-19. CRRT is applied frequently in severe COVID-19 patients than that in nonsevere COVID-19 patients. The risk of AKI is higher in the critical group than that in the severe group.

4. **Delirium in Patients with SARS-CoV-2 Infection: A Multicenter Study.** Reborá P, Rozzini R, Bianchetti A, et al. *J Am Geriatr Soc*. 2020 Nov 27. doi: 10.1111/jgs.16969.

<https://agsjournals.onlinelibrary.wiley.com/doi/10.1111/jgs.16969>

Findings: Overall, 73 (14.1%) patients presented delirium on admission. Factors significantly associated with delirium were dementia, the number of chronic diseases, and chest X-ray or CT opacity. There were 148 (33.4%) in-hospital deaths in the no-delirium group and 43 (58.9%) in the delirium group. Delirium is prevalent and associated with in-hospital mortality among older patients hospitalized with SARS-CoV-2 infection.

5. **Prevalence and risk factors for delirium in critically ill patients with COVID-19 (COVID-D): a multicentre cohort study.** Pun BT et al. *Lancet* 2021 Jan 8. doi: 10.1016/S2213-2600(20)30552-X [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30552-X/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30552-X/fulltext)

Findings: This multicentre cohort study included 69 adult ICUs, across 14 countries. We included all patients (aged  $\geq 18$  years) admitted to participating ICUs with severe acute respiratory syndrome coronavirus 2 infection before April 28, 2020. Between Jan 20 and April 28, 2020, 4530 patients with COVID-19 were admitted to 69 ICUs, of whom 2088 patients were included in the study cohort. The median age of patients was 64 years with a median Simplified Acute Physiology Score (SAPS) II of 40.0. 1397 (66.9%) of 2088 patients were invasively mechanically ventilated on the day of ICU admission and 1827 (87.5%) were invasively mechanical ventilated at some point during hospitalisation. Infusion with sedatives while on mechanical ventilation was common: 1337 (64.0%) of 2088 patients were given benzodiazepines for a median of 7.0 days and 1481 (70.9%) were given propofol for a median of 7.0 days. Median Richmond Agitation–Sedation Scale score while on invasive mechanical

ventilation was –4. 1704 (81.6%) of 2088 patients were comatose for a median of 10.0 days and 1147 (54.9%) were delirious for a median of 3.0 days. Mechanical ventilation, use of restraints, and benzodiazepine, opioid, and vasopressor infusions, and antipsychotics were each associated with a higher risk of delirium the next day, whereas family visitation (in person or virtual) was associated with a lower risk of delirium. During the 21-day study period, patients were alive without delirium or coma for a median of 5.0 days. At baseline, older age, higher SAPS II scores, male sex, smoking or alcohol abuse, use of vasopressors on day 1, and invasive mechanical ventilation on day 1 were independently associated with fewer days alive and free of delirium and coma. 601 (28.8%) of 2088 patients died within 28 days of admission, with most of those deaths occurring in the ICU. Acute brain dysfunction was highly prevalent and prolonged in critically ill patients with COVID-19. Benzodiazepine use and lack of family visitation were identified as modifiable risk factors for delirium, and thus these data present an opportunity to reduce acute brain dysfunction in patients with COVID-19.

### Diagnosics & Screening

6. **Evaluation of a rapid antigen test (Panbio™ COVID-19 Ag rapid test device) for SARS-CoV-2 detection in asymptomatic close contacts of COVID-19 patients.** Torres I, Poujois S, Albert E, et al. *Clin Microbiol Infect.* 2021 Jan 6:S1198-743X(20)30782-5. doi: 10.1016/j.cmi.2020.12.022. [https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(20\)30782-5/fulltext](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30782-5/fulltext)  
Findings: A total of 634 individuals were enrolled. Two nasopharyngeal swabs were collected from household (n=338) and non-household contacts (n=296) of COVID-19 cases. RAD testing was carried out at the point of care. The RT-PCR test used was the TaqPath COVID-19 Combo Kit. Household contacts were tested at a median of 2 days after diagnosis of the index case, whereas non-household contacts (n=296) were tested at a median of 6 days after exposure. In total, 79 individuals (12.4%) tested positive by RT-PCR, of whom 38 (48.1%) yielded positive RAD results. The overall sensitivity and specificity of the RAD test was 48.1% (95% CI: 37.4-58.9) and 100% (95% CI: 99.3-100), respectively. Sensitivity was higher in household (50.8%; 95% CI: 38.9-62.5) than in non-household (35.7%; 95% CI:16.3-61.2%) contacts. Individuals testing positive by RAD test were more likely (P<0.001) to become symptomatic than their negative counterparts. The Panbio test displays low sensitivity in asymptomatic close contacts of COVID-19 patients, particularly in non-household contacts. Nonetheless, establishing the optimal timing for upper respiratory tract collection in this group seems imperative to pinpoint test sensitivity.
7. **The Sensitivity and Costs of Testing for SARS-CoV-2 Infection with Saliva Versus Nasopharyngeal Swabs: A Systematic Review and Meta-analysis.** Bastos ML, Perlman-Arrow S, et al. *Ann Intern Med.* 2021 Jan 12. doi: 10.7326/M20-6569. <https://www.acpjournals.org/doi/10.7326/M20-6569>  
Findings: Thirty-seven studies with 7332 paired samples were included. Against a reference standard of a positive result on either sample, the sensitivity of saliva was 3.4 percentage points lower than that of nasopharyngeal swabs. Among persons with previously confirmed SARS-CoV-2 infection, saliva's sensitivity was 1.5 percentage points higher than that of nasopharyngeal swabs. Among persons without a previous SARS-CoV-2 diagnosis, saliva was 7.9 percentage

points less sensitive. In this subgroup, if testing 100 000 persons with a SARS-CoV-2 prevalence of 1%, nasopharyngeal swabs would detect 79 more persons with SARS-CoV-2 than saliva, but with an incremental cost per additional infection detected of \$8093. Saliva sampling seems to be a similarly sensitive and less costly alternative that could replace nasopharyngeal swabs for collection of clinical samples for SARS-CoV-2 testing.

## Epidemiology & Public Health

8. **What have we learned about positive changes experienced during COVID-19 lockdown? Evidence of the social patterning of change.** Williams L, Rollins L, Young D. *PLoS One*. 2021 Jan 5;16(1):e0244873. doi: 10.1371/journal.pone.0244873.  
<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0244873>  
Findings: Multiple studies have highlighted the negative impact of COVID-19. Complementing this work, here, we report on the social patterning of self-reported positive changes experienced during COVID-19 national lockdown in Scotland. The CATALYST study collected data from 3342 adults in Scotland during weeks 9-12 of a national lockdown. Using a cross-sectional design, participants completed an online questionnaire providing data on key sociodemographic and health variables and completed a measure of positive change. The positive change measure spanned diverse domains (e.g., more quality time with family, developing new hobbies, more physical activity, and better quality of sleep). We used univariate analysis and stepwise regression to examine the contribution of a range of sociodemographic factors (e.g., age, gender, ethnicity, educational attainment, and employment status) in explaining positive change. There were clear sociodemographic differences across positive change scores. Those reporting higher levels of positive change were female, from younger age groups, married or living with their partner, employed, and in better health. Overall our results highlight the social patterning of positive changes during lockdown in Scotland. These findings begin to illuminate the complexity of the unanticipated effects of national lockdown and will be used to support future intervention development work sharing lessons learned from lockdown to increase positive health change amongst those who may benefit.
  
9. **The Immediate Effect of COVID-19 Policies on Social-Distancing Behavior in the United States.** Abouk R, Heydari B. *Public Health Rep*. 2021 Jan 5:33354920976575. doi: 10.1177/0033354920976575.  
<https://journals.sagepub.com/doi/epub/10.1177/0033354920976575>  
Findings: We applied difference-in-differences and event-study methodologies to evaluate the effect of the 6 social-distancing policies on Google-released aggregated, anonymized daily location data on movement trends over time by state for all 50 states and the District of Columbia in 6 location categories: retail and recreation, grocery stores and pharmacies, parks, transit stations, workplaces, and residences. We compared the outcome of interest in states that adopted COVID-19-related policies with states that did not adopt such policies, before and after these policies took effect during February 15-April 25, 2020. Statewide stay-at-home orders had the strongest effect on reducing out-of-home mobility and increased the time people spent at home by an estimated 2.5 percentage points (15.2%) from before to after

policies took effect. Limits on restaurants and bars ranked second and resulted in an increase in presence at home by an estimated 1.4 percentage points (8.5%). The other 4 policies did not significantly reduce mobility. Statewide stay-at-home orders and limits on bars and restaurants were most closely linked to reduced mobility in the early stages of the COVID-19 pandemic, whereas the potential benefits of other such policies may have already been reaped from voluntary social distancing. Further research is needed to understand how the effect of social-distancing policies changes as voluntary social distancing wanes during later stages of a pandemic.

**10. Assessing Mandatory Stay-at-Home and Business Closure Effects on the Spread of COVID-19.**

Bendavid E, Oh C, Bhattacharya J, Ioannidis JPA. *Eur J Clin Invest.* 2021 Jan 5:e13484. doi: 10.1111/eci.13484. <https://onlinelibrary.wiley.com/doi/10.1111/eci.13484>

Findings: We first estimate COVID-19 case growth in relation to any NPI implementation in subnational regions of 10 countries: England, France, Germany, Iran, Italy, Netherlands, Spain, South Korea, Sweden, and the US. Using first-difference models with fixed effects, we isolate the effects of mrNPIs by subtracting the combined effects of lrNPIs and epidemic dynamics from all NPIs. We use case growth in Sweden and South Korea, two countries that did not implement mandatory stay-at-home and business closures, as comparison countries for the other 8 countries (16 total comparisons). Implementing any NPIs was associated with significant reductions in case growth in 9 out of 10 study countries, including South Korea and Sweden that implemented only lrNPIs (Spain had a non-significant effect). After subtracting the epidemic and lrNPI effects, we find no clear, significant beneficial effect of mrNPIs on case growth in any country. In France, e.g., the effect of mrNPIs was +7% (95CI -5%-19%) when compared with Sweden, and +13% (-12%-38%) when compared with South Korea (positive means pro-contagion). The 95% confidence intervals excluded 30% declines in all 16 comparisons and 15% declines in 11/16 comparisons. While small benefits cannot be excluded, we do not find significant benefits on case growth of more restrictive NPIs. Similar reductions in case growth may be achievable with less restrictive interventions.

**11. Predictors of mortality of COVID-19 in the general population and nursing homes.** España PP, Bilbao A, García-Gutiérrez S, et al. *Intern Emerg Med.* 2021 Jan 5. doi: 10.1007/s11739-020-02594-8. <https://link.springer.com/article/10.1007/s11739-020-02594-8>

Findings: The goal of the study was to identify factors associated with risk of death among patients with COVID-19. In the multivariable model based on nursing home residents, predictors of mortality were being male, older than 80 years, admitted to a hospital for COVID-19, and having cardiovascular disease, kidney disease or dementia while taking anticoagulants or lipid-lowering drugs at baseline was protective. The AUC was 0.754 for the risk score based on this model and 0.717 in the validation subsample. Predictors of death among people from the general population were being male and/or older than 60 years, having been hospitalized in the month before admission for COVID-19, being admitted to a hospital for COVID-19, having cardiovascular disease, dementia, respiratory disease, liver disease, diabetes with organ damage, or cancer while being on anticoagulants was protective. The AUC was 0.941 for this model's risk score and 0.938 in the validation subsample. Our risk scores could help physicians

identify high-risk groups and establish preventive measures and better follow-up for patients at high risk of dying.

12. **Estimation of US SARS-CoV-2 Infections, Symptomatic Infections, Hospitalizations, and Deaths Using Seroprevalence Surveys.** Angulo FJ, Finelli L, Swerdlow DL. *JAMA Netw Open*. 2021 Jan 4;4(1):e2033706. doi: 10.1001/jamanetworkopen.2020.33706.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2774584>

Findings: Adjusting reported COVID-19 infections using underreporting multipliers derived from CDC seroprevalence studies in April (n = 16 596), May (n = 14 291), June (n = 14 159), July (n = 12 367), and August (n = 38 355), there were estimated medians of 46 910 006 SARS-CoV-2 infections, 28 122 752 symptomatic infections, 956 174 hospitalizations, and 304 915 deaths in the US through November 15, 2020. An estimated 14.3% of the US population were infected by SARS-CoV-2 as of mid-November 2020. The SARS-CoV-2 disease burden may be much larger than reported COVID-19 cases owing to underreporting. Even after adjusting for underreporting, a substantial gap remains between the estimated proportion of the population infected and the proportion infected required to reach herd immunity. Additional seroprevalence surveys are needed to monitor the pandemic, including after the introduction of safe and efficacious vaccines.

13. **Assessment of Day-7 Postexposure Testing of Asymptomatic Contacts of COVID-19 Patients to Evaluate Early Release from Quarantine - Vermont, May-November 2020.** Jones A, Fialkowski V, Prinzing L, et al. *MMWR Morb Mortal Wkly Rep*. 2021 Jan 8;70(1):12-13. doi:

10.15585/mmwr.mm7001a3. <https://www.cdc.gov/mmwr/volumes/70/wr/mm7001a3.htm>

Findings: Our results indicate that among the persons in quarantine who tested negative at day 7 after exposure, none who were retested between day 8 and 14 were positive. Allowing asymptomatic persons to shorten quarantine with a negative test at day 7 or later has not been demonstrated to result in transmission of SARS-CoV-2, indicating that the policy has been effective. These results also indicate that 3.9% of contacts tested on days 7–10 after exposure were infected with SARS-CoV-2. In addition to reducing the duration of quarantine for exposed contacts, Vermont’s policy might have provided additional benefits to the state’s pandemic response by identifying some asymptomatic patients earlier in the course of their illness through enhancing statewide surveillance testing of an exposed group. This assessment supports Vermont’s policy as being effective and offers data to support recommendations to shorten quarantine with testing such as those provided in CDC’s updated quarantine guidance.

14. **Impact of the Coronavirus Disease 2019 Pandemic on Outpatient Antibiotic Prescriptions in the United States.** Buehrle DJ, Nguyen MH, Wagener MM, Clancy CJ. *Open Forum Infect Dis*. 2020 Dec 22;7(12):ofaa575. doi: 10.1093/ofid/ofaa575.

<https://academic.oup.com/ofid/article/7/12/ofaa575/6043456>

Findings: In April 2020, there were significant reductions in prescription fills of each of the 10 most prescribed outpatient antibiotics in the United States. Monthly azithromycin, amoxicillin-clavulanate, and levofloxacin fills did not rebound significantly from April through July 2020. Coronavirus disease 2019 had an immediate and sustained impact on US outpatient antibiotic prescribing.



15. **Incidence and Secondary Transmission of SARS-CoV-2 Infections in Schools.** Zimmerman KO, Akinboyo IC, Brookhart MA, et al. *Pediatrics*. 2021 Jan 8:e2020048090. doi: 10.1542/peds.2020-048090.

<https://pediatrics.aappublications.org/content/pediatrics/early/2021/01/06/peds.2020-048090.full.pdf>

Findings: In the first 9 weeks of in-person instruction in North Carolina schools, we found extremely limited within-school secondary transmission of SARS-CoV-2, determined by contact tracing. The frequency of within-school transmission of SARS-CoV-2 with in-person instruction in communities with widespread transmission is unknown. Many school districts across the United States are currently deciding whether or not to reopen for in-person learning for the second semester. We examined 11 school districts with nearly 100,000 students/staff open for 9 weeks of in-person instruction, tracking secondary transmission of SARS-CoV-2; within-school infections were extremely rare. Each case was independently adjudicated for community or within-school acquisition by local health departments.

16. **The impact of statewide school closures on COVID-19 infection rates.** Staguhn ED, Castillo RC, Weston-Farber E. *Am J Infect Control*. 2021 Jan 8:S0196-6553(21)00001-8. doi:

10.1016/j.ajic.2021.01.002. [https://www.ajicjournal.org/article/S0196-6553\(21\)00001-8/fulltext](https://www.ajicjournal.org/article/S0196-6553(21)00001-8/fulltext)

Findings: Daily COVID-19 infection rates were examined before and after statewide school closure orders. Regression techniques were used to model changes in the number of confirmed cases and data was combined across states using meta analyses. School closures were found to have a significant impact on infection rates, and thus, may be considered a viable intervention to lower COVID-19 infection rates.

### **Healthcare Delivery & Healthcare Workers**

17. **The duration, dynamics and determinants of SARS-CoV-2 antibody responses in individual healthcare workers.** Lumley SF, Wei J, O'Donnell D, et al. *Clin Infect Dis*. 2021 Jan 6:ciab004. doi: 10.1093/cid/ciab004. [https://academic.oup.com/cid/advance-](https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab004/6064824)

[article/doi/10.1093/cid/ciab004/6064824](https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab004/6064824)

Findings: We present 6 months of data from a longitudinal seroprevalence study of 3276 UK HCWs. Serial measurements of SARS-CoV-2 anti-nucleocapsid and anti-spike IgG were obtained. Anti-spike IgG levels remained stably detected after a positive result, e.g., in 94% of HCWs at 180 days. Anti-nucleocapsid IgG levels rose to a peak at 24 days post first PCR-positive test, before beginning to fall. Considering 452 anti-nucleocapsid seropositive HCWs over a median of 121 days from their maximum positive IgG titre, the mean estimated antibody half-life was 85 days. Higher maximum observed anti-nucleocapsid titres were associated with longer estimated antibody half-lives. Increasing age, Asian ethnicity and prior self-reported symptoms were independently associated with higher maximum anti-nucleocapsid levels and increasing age and a positive PCR test undertaken for symptoms with longer anti-nucleocapsid half-lives. SARS-CoV-2 anti-nucleocapsid antibodies wane within months, and faster in younger adults and those without symptoms. However, anti-spike IgG remains stably detected. Ongoing

longitudinal studies are required to track the long-term duration of antibody levels and their association with immunity to SARS-CoV-2 reinfection.

18. **Medicaid Expansion: Effects on Hospital Finances and Implications for Hospitals Facing COVID-19 Challenges.** Blavin F, Ramos C. *Health Aff (Millwood)*. 2021 Jan;40(1):82-90. doi: 10.1377/hlthaff.2020.00502.

<https://www.healthaffairs.org/doi/abs/10.1377/hlthaff.2020.00502>

Findings: States' decisions to expand Medicaid may have important implications for their hospitals' financial ability to weather the coronavirus disease 2019 (COVID-19) pandemic. This study estimated the effects of the Affordable Care Act (ACA) Medicaid expansion on hospital finances in 2017 to update earlier findings. The analysis also explored how the ACA Medicaid expansion affects different types of hospitals by size, ownership, rurality, and safety-net status. We found that the early positive financial impact of Medicaid expansion was sustained in fiscal years 2016 and 2017 as hospitals in expansion states continued to experience decreased uncompensated care costs and increased Medicaid revenue and financial margins. The magnitude of these impacts varied by hospital type. As COVID-19 has brought hospitals to a time of great need, findings from this study provide important information on what hospitals in states that have yet to expand Medicaid could gain through expansion and what is at risk should any reversal of Medicaid expansions occur.

19. **Infectivity of Healthcare Workers Diagnosed with SARS-CoV-2 Infection Approximately 2 weeks after Onset of Symptoms: A Cross-Sectional Study.** Longtin Y, Charest H, Quach C, et al. *Infect Control Hosp Epidemiol*. 2021 Jan 11:1-9. doi: 10.1017/ice.2020.1420.

<https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/infectivity-of-healthcare-workers-diagnosed-with-sarscov2-infection-approximately-2-weeks-after-onset-of-symptoms-a-crosssectional-study/DE4CD62A4F77591E52AF0BE53518BDD8>

Findings: We performed viral culture of respiratory specimens in 118 SARS-CoV-2 infected healthcare workers (HCW), approximately 2 weeks after symptom onset. Only one HCW (0.8%) had a positive culture. No factors for prolonged viral shedding were identified. Infectivity is resolved in nearly all HCWs approximately 2 weeks after symptom onset.

### Laboratory Results

20. **Changes in the humoral immunity response in SARS-CoV-2 convalescent patients over 8 months.** Peng P, Hu J, Deng HJ, et al. *Cell Mol Immunol*. 2021 Jan 8:1-2. doi: 10.1038/s41423-020-00605-4. <https://www.nature.com/articles/s41423-020-00605-4>

Findings: Twenty patients who had recovered from COVID-19 were included in our cohort. Blood samples were obtained in February and October, corresponding to a median of 25 (range 5–33 days) and 230 (range 221–248 days) days after symptom onset. Enzyme-linked immunosorbent assay was performed to evaluate the presence of anti-SARS-CoV-2 spike receptor-binding domain (RBD) IgG over 8 months. A preliminary positive cutoff was set with the mean value of negative controls above 3 standard deviations. Neutralizing antibodies (NAbs) were measured by pseudovirus-based assays associated with two SARS-CoV-2 strains (S-



D614 and S-G614) in 293T-ACE2 cells. The 50% inhibitory dose (ID50) was calculated as the NAb titer.

## Prognosis

- 21. Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers and the Risk of SARS-CoV-2 Infection or Hospitalization with COVID-19 Disease: A Systematic Review and Meta-Analysis.** Tleyjeh IM, Bin Abdulhak AA, et al. [*Providence Author*]. *Am J Ther.* 2020 Dec 28. doi: 10.1097/MJT.0000000000001319

[https://journals.lww.com/americantherapeutics/Abstract/9000/Angiotensin\\_Converting\\_Enzyme\\_Inhibitors\\_and.98154.aspx](https://journals.lww.com/americantherapeutics/Abstract/9000/Angiotensin_Converting_Enzyme_Inhibitors_and.98154.aspx)

Findings: Ten studies (6 cohorts and 4 case control) that enrolled a total of 23,892 patients and 853,369 controls were eligible for inclusion in our meta-analysis. One study was excluded from the analysis because of high risk of bias. Prior use of ACEIs was not associated with an increased risk of acquiring SARS-CoV-2 or hospitalization due to COVID-19 disease, odds ratio 0.98, 95% confidence interval (0.91-1.05), I<sup>2</sup> = 15%. Similarly, prior use of ARBs was not associated with an increased risk of acquiring SARS-CoV-2, odds ratio 1.04, 95% confidence interval (0.98-1.10), I<sup>2</sup> = 0%. Cumulative evidence suggests that prior use of ACEIs or ARBs is not associated with a higher risk of COVID-19 or hospitalization due to COVID-19 disease. Our results provide a reassurance to the public not to discontinue prescribed ACEIs/ARBs because of fear of COVID-19.

- 22. Prevalence and 6-month recovery of olfactory dysfunction: a multicentre study of 1363 COVID-19 patients.** Lechien JR, Chiesa-Estomba CM, Beckers E, et al. *J Intern Med.* 2021 Jan 5. doi: 10.1111/joim.13209. <https://onlinelibrary.wiley.com/doi/10.1111/joim.13209>

Findings: To investigate prevalence and recovery of OD in COVID-19 patients according to the disease severity. From 22 March to 3 June 2020, 2581 COVID-19 patients were identified from 18 European hospitals. The prevalence of OD was significantly higher in mild form (85.9%) compared with moderate-to-critical forms (4.5-6.9%). Of the 1916 patients with OD, 1363 completed the evaluations (71.1%). A total of 328 patients (24.1%) did not subjectively recover olfaction 60 days after the onset of the dysfunction. OD is more prevalent in mild COVID-19 forms than in moderate-to-critical forms. OD disappeared in 95% of patients regarding objective olfactory evaluations at 6 months.

- 23. Full Inequities in Diabetic Ketoacidosis among Patients with Type 1 diabetes and COVID-19: Data from 52 US Clinical Centers.** Ebekeozien O, Agarwal S, Noor N, et al. *J Clin Endocrinol Metab.* 2021 Jan 7:dga920. doi: 10.1210/clinem/dga920.

<https://academic.oup.com/jcem/advance-article/doi/10.1210/clinem/dga920/6042218>

Findings: This is a cross-sectional study of patients with T1D and laboratory-confirmed COVID-19 from 52 clinical sites in the US, data was collected April - August 2020. We examined the distribution of patient factors and DKA events across NH White, NH Black, and Hispanic race/ethnicity groups. Multivariable logistic regression analysis was performed to examine the odds of DKA among NH Black and Hispanic patients with T1D as compared to NH White patients, adjusting for potential confounders, such as age, sex, insurance, and last HbA1c. We

included 180 patients with T1D and laboratory-confirmed COVID-19 in the analysis. Forty-four percent were NH White, 31% NH Black, 26% Hispanic. NH Blacks and Hispanics had higher median HbA1c than Whites. We found that more NH Black and Hispanic presented with DKA compared to Whites (55% and 33% vs. 13%). After adjusting for potential confounders, NH Black patients continued to have greater odds of presenting with DKA compared with NH Whites. We found that among T1D patients with COVID-19 infection, NH Blacks were more likely to present in DKA compared with NH White patients. Our findings demonstrate additional risk among NH Blacks with T1D and COVID-19.

24. **Association Between Chronic Use of Immunosuppressive Drugs and Clinical Outcomes from Coronavirus Disease 2019 (COVID-19) Hospitalization: A Retrospective Cohort Study in a Large US Health System.** Andersen KM, Mehta HB, Palamuttam N, et al. *Clin Infect Dis.* 2021 Jan 7:ciaa1488. doi: 10.1093/cid/ciaa1488. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1488/6067567>

Findings: Retrospective cohort study in 2121 consecutive adults with acute inpatient hospital admission between 4 March and 29 August 2020 with confirmed or suspected COVID-19 in a large academic health system. There were 2121 patients admitted with laboratory-confirmed (1967, 93%) or suspected (154, 7%) COVID-19 during the study period, with a median age of 55 years. Of these, 108 (5%) were classified as immunosuppressed before COVID-19, primarily with prednisone (>7.5 mg/day), tacrolimus, or mycophenolate mofetil. Among the entire cohort, 311 (15%) received mechanical ventilation; the median length of stay was 5.2 days, and 1927 (91%) survived to discharge. After adjustment, there were no significant differences in the risk of mechanical ventilation, in-hospital mortality, or length of stay among individuals with immunosuppression and counterparts. Chronic use of immunosuppressive drugs was neither associated with worse nor better clinical outcomes among adults hospitalized with COVID-19 in one US health system.

25. **Outcomes of COVID-19 in hospitalized solid organ transplant recipients compared to a matched cohort of non-transplant patients at a national healthcare system in the United States.** Fisher AM, Schlauch D, Mulloy M, et al. *Clin Transplant.* 2021 Jan 6:e14216. doi: 10.1111/ctr.14216. <https://onlinelibrary.wiley.com/doi/abs/10.1111/ctr.14216>

Findings: Data describing outcomes of solid organ transplant (SOT) recipients with COVID-19 are variable, and the association between SOT status and mortality remains unclear. In this study, we compare clinical outcomes of SOT recipients hospitalized with COVID-19 between March 10 and September 1, 2020 to a matched cohort of non-SOT recipients at a national healthcare system in the US. From a population of 43,461 hospitalized COVID-19 positive patients, we created a coarsened exact matched cohort of 4,035 patients including 128 SOT recipients and 3,907 weighted matched non-SOT controls. Multiple logistic regression was used to evaluate association between SOT status and clinical outcomes. Among the 4,035 patients, median age was 60 years, 61.7% were male, 21.9% were Black/African American, and 50.8% identified as Hispanic/Latino ethnicity. Patients with a history of SOT were more likely to die within the study period when compared to matched non-SOT recipients (21.9% and 14.9%). Moreover, SOT status was associated with increased odds of receiving invasive mechanical ventilation, developing acute kidney injury, and receiving vasopressor support during hospitalization.

26. **Sixty-Day Mortality among 520 Italian Hospitalized COVID-19 Patients According to the Adopted Ventilatory Strategy in the Context of an Integrated Multidisciplinary Clinical Organization: A Population-Based Cohort Study.** Potalivo A, Montomoli J, Facondini F, et al. *Clin Epidemiol.* 2020 Dec 30;12:1421-1431. doi: 10.2147/CLEP.S278709.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7779307/>

Findings: All COVID-19 patients (26/02/2020-18/04/2020) in the Rimini Province of Italy were included in this population-based cohort study. The hospitalized patients were classified according to the maximum level of respiratory support: oxygen supplementation (Oxygen group), non-invasive ventilation (NIV-only group), invasive mechanical ventilation (IMV-only group), and IMV after an NIV trial (IMV-after-NIV group). We identified a total of 1,424 symptomatic patients: 520 (36.5%) were hospitalized, while 904 (63.5%) were treated at home with no 60-day deaths. Based on the respiratory support, 408 (78.5%) were assigned to the Oxygen group, 46 (8.8%) to the NIV-only group, 25 (4.8%) to the IMV-after-NIV group, and 41 (7.9%) to the IMV-only group. There was no significant difference in the PaO<sub>2</sub>/FiO<sub>2</sub> at IMV inception in the IMV-after-NIV and IMV-only groups (p=0.9). Overall 60-day mortality was 24.2% (Oxygen: 23.0%; NIV-only: 19.6%; IMV-after-NIV: 32.0%; IMV-only: 36.6%; p=0.165). Compared with the Oxygen group, the adjusted 60-day mortality risk significantly increased in the IMV-after-NIV (HR 2.776; p=0.024) and IMV-only groups (HR 2.966; p=0.001). This study provided a population-based estimate of the impact of the COVID-19 outbreak in a severely affected Italian province. A similar 60-day mortality risk was found for patients undergoing immediate IMV and those intubated after an NIV trial with favorable outcomes after prolonged IMV.

27. **Clinical Outcomes of Coronavirus Disease 2019 (COVID-19) Positive Patients Who Underwent Surgery: A New York City Experience.** Vranis NM, Bekisz JM, Daar DA, et al. *J Surg Res.* 2020 Nov 23;261:113-122. doi: 10.1016/j.jss.2020.10.032.

<https://www.sciencedirect.com/science/article/pii/S0022480420308131>

Findings: A retrospective review was performed of all COVID-19, positive with PCR confirmation, patients who had surgery between February 17, 2020 and April 26, 2020 at a major New York City hospital. Clinical characteristics and outcomes including ICU admission, ventilator requirement, and mortality were analyzed. Thirty-nine COVID-19 surgical patients were identified. Mean age was 53.9 y, and there were more men than women in the cohort (56.4% versus 43.6%). Twenty-two patients (56.4%) had a confirmed positive COVID-19 test preoperatively, and the remainder tested positive after their procedure. The majority (59%) of patients had an American Society of Anesthesiologists (ASA) class of 3 or higher. Postoperatively, 7 patients (17.9%) required ICU level care with a mean length of stay of 7.7 d. There were 4 deaths (10.3%) in this patient population, all of which occurred in patients who were ASA class 3 or 4. This study represents the largest study to date, that objectively analyzes the outcomes of COVID-19 positive patients who underwent surgery. Overall, ICU admission rates and mortality are similar to reported rates in the literature for nonsurgical COVID-19 patients. Notably, in COVID-19 patients with ASA 1 or 2, there was a 0% mortality rate in the postoperative period.

28. **Risk factors of viral RNAemia and its association with clinical prognosis among patients with severe COVID-19.** Li H, Gu X, Li H, et al. *Chest*. 2021 Jan 6:S0012-3692(21)00007-6. doi: 10.1016/j.chest.2020.11.071. [https://journal.chestnet.org/article/S0012-3692\(21\)00007-6/pdf](https://journal.chestnet.org/article/S0012-3692(21)00007-6/pdf)  
Findings: our study revealed that a high percentage of severe COVID-19 patients complicated with viral RNAemia, which is significantly associated with worse outcomes. Patients with more severe baseline disease condition and prior corticosteroids therapy for underlying diseases have higher risk of developing viral RNAemia. Our data benefit a better understanding of pathogenesis of COVID-19 and provide a basis for the early identification and management of critically ill patients.
29. **Risk Factors for Mortality and Progression to Severe COVID-19 Disease in the Southeast United States (US): A Report from the SEUS Study Group.** Hobbs ALV, Turner N, Omer I, et al. *Infect Control Hosp Epidemiol*. 2021 Jan 11:1-33. doi: 10.1017/ice.2020.1435. <https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/risk-factors-for-mortality-and-progression-to-severe-covid19-disease-in-the-southeast-united-states-us-a-report-from-the-seus-study-group/AF749E8B74FC19759A3CDB787479A6E5>  
Findings: A total of 502 patients were included. Hospital mortality was 16% (76/476), while 35% (177/502) required ICU admission, and 18% (91/502) required mechanical ventilation. By both univariate and adjusted multivariate analysis, hospital mortality was independently associated with age, male sex, and cardiovascular disease. As with mortality, risk of severe disease was independently associated with age, male sex, and cardiovascular disease. In an adjusted multivariate analysis, advanced age, male sex, and cardiovascular disease increased risk of severe disease and mortality in patients with COVID-19 in the Southeast US. In-hospital mortality risk doubled with each subsequent decade of life.

### Survivorship & Rehabilitation

30. **6-month consequences of COVID-19 in patients discharged from hospital: a cohort study.** Huang C et al. *Lancet* 2021 Jan 8. [https://doi.org/10.1016/S0140-6736\(20\)32656-8](https://doi.org/10.1016/S0140-6736(20)32656-8)  
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)32656-8/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32656-8/fulltext)  
Findings: In total, 1733 of 2469 discharged patients with COVID-19 were enrolled after 736 were excluded. Patients had a median age of 57.0 years and 897 (52%) were men. The median follow-up time after symptom onset was 186.0 days. At 6 months after acute infection, COVID-19 survivors were mainly troubled with fatigue or muscle weakness, sleep difficulties, and anxiety or depression. Patients who were more severely ill during their hospital stay had more severe impaired pulmonary diffusion capacities and abnormal chest imaging manifestations and are the main target population for intervention of long-term recovery.
31. **Pulmonary function and radiological features four months after COVID-19: first results from the national prospective observational Swiss COVID-19 lung study.** Guler SA, Ebner L, Beigelman C, et al. *Eur Respir J*. 2021 Jan 8:2003690. doi: 10.1183/13993003.03690-2020. <https://erj.ersjournals.com/content/early/2020/12/17/13993003.03690-2020>

Findings: 113 COVID-19 survivors were included (mild/moderate 47, severe/critical 66). We confirmed several comorbidities as risk factors for severe/critical disease. Four months after SARS CoV-2 infection, severe/critical COVID-19 was associated with significant functional and radiological abnormalities, potentially due to small airway and lung parenchymal disease. A systematic follow-up for survivors needs to be evaluated to optimise care for patients recovering from COVID-19.

## Therapeutics

32. **Efficacy and Safety of Tocilizumab for Coronavirus Disease 2019 (Covid-19) Patients: A Systematic Review and Meta-analysis.** Hariyanto TI, Hardyson W, Kurniawan A. *Drug Res (Stuttg)*. 2021 Jan 5. doi: 10.1055/a-1336-2371. <https://www.thieme-connect.com/products/ejournals/abstract/10.1055/a-1336-2371?device=mobile>

Findings: A total of 38 studies with a total of 13 412 COVID-19 patients were included in our analysis. Our meta-analysis showed that tocilizumab treatment is associated with reduction of mortality rate from COVID-19, but did not alter the severity of COVID-19, and length of hospital stay. Tocilizumab also does not associated with serious adverse events compared with standard of care treatment. Our study does not support the routine use of tocilizumab for COVID-19 patients. Future studies should focus more on other potential therapies for COVID-19 patients.

33. **Umbilical cord mesenchymal stem cells for COVID-19 acute respiratory distress syndrome: A double-blind, phase 1/2a, randomized controlled trial.** Lanzoni G, Linetsky E, Correa D, et al. *Stem Cells Transl Med*. 2021 Jan 5. doi: 10.1002/sctm.20-0472. <https://stemcellsjournals.onlinelibrary.wiley.com/doi/10.1002/sctm.20-0472>

Findings: The objective of this study was to determine safety and explore efficacy of umbilical cord mesenchymal stem cell (UC-MSC) infusions in subjects with COVID-19 ARDS. A double-blind, phase 1/2a, randomized, controlled trial was performed. Twenty-four subjects were randomized 1:1 to either UC-MSC treatment (n = 12) or the control group (n = 12). Subjects in the UC-MSC treatment group received two intravenous infusions (at day 0 and 3) of  $100 \pm 20 \times 10^6$  UC-MSCs; controls received two infusions of vehicle solution. Both groups received best standard of care. No difference was observed between groups in infusion-associated AEs. No serious adverse events (SAEs) were observed related to UC-MSC infusions. UC-MSC infusions in COVID-19 ARDS were found to be safe. Inflammatory cytokines were significantly decreased in UC-MSC-treated subjects at day 6. Treatment was associated with significantly improved patient survival (91% vs 42%, P = .015), SAE-free survival (P = .008), and time to recovery (P = .03). UC-MSC infusions are safe and could be beneficial in treating subjects with COVID-19 ARDS.

34. **Tracheotomy in COVID-19 Patients: A Systematic Review and Meta-analysis of Weaning, Decannulation, and Survival.** Benito DA, Bestourous DE, Tong JY, Pasick LJ, Sataloff RT. *Otolaryngol Head Neck Surg*. 2021 Jan 5:194599820984780. doi: 10.1177/0194599820984780. <https://journals.sagepub.com/doi/epub/10.1177/0194599820984780>

Findings: After identifying 232 unique studies, 18 articles encompassing outcomes for 3234 patients were ultimately included for meta-analysis, with a weighted mean follow-up time of



28.6 ± 6.2 days after tracheotomy. Meta-analysis revealed that 55.0% of tracheotomized patients were weaned successfully from mechanical ventilation. Approximately 34.9% of patients were decannulated successfully, with a mean decannulation time of 18.6 ± 5.7 days after tracheotomy. The pooled mortality in tracheotomized patients with COVID-19 was 13.1%, with a mean time of death of 13.0 ± 4.0 days following tracheotomy. At the current state of the coronavirus pandemic, over half of patients who have required tracheotomies are being weaned off of mechanical ventilation. While 13.1% patients have died prior to decannulation, over a third of all tracheotomized patients with COVID-19 reported in the literature have undergone successful decannulation.

35. **Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults.** Libster R, Pérez Marc G, Wappner D, et al. *NEJM* January 6, 2021 DOI: 10.1056/NEJMoa2033700 <https://www.nejm.org/doi/full/10.1056/NEJMoa2033700?query=TOC>

Findings: Therapies to interrupt the progression of early Covid-19 remain elusive. Among them, convalescent plasma administered to hospitalized patients has been unsuccessful, perhaps because antibodies should be administered earlier in the course of illness. We conducted a randomized, double-blind, placebo-controlled trial of convalescent plasma with high IgG titers against SARS-CoV-2 in older adult patients within 72 hours after the onset of mild Covid-19 symptoms. The primary end point was severe respiratory disease, defined as a respiratory rate of 30 breaths per minute or more, an oxygen saturation of less than 93% while the patient was breathing ambient air, or both. The trial was stopped early at 76% of its projected sample size because cases of Covid-19 in the trial region decreased considerably and steady enrollment of trial patients became virtually impossible. A total of 160 patients underwent randomization. In the intention-to-treat population, severe respiratory disease developed in 13 of 80 patients (16%) who received convalescent plasma and 25 of 80 patients (31%) who received placebo, with a relative risk reduction of 48%. Early administration of high-titer convalescent plasma against SARS-CoV-2 to mildly ill infected older adults reduced the progression of Covid-19.

36. **Heparin in COVID-19 patients is associated with reduced in-hospital mortality: the multicentre Italian CORIST Study.** Di Castelnuovo AF, Costanzo S, Iacoviello L. *Thromb Haemost.* 2021 Jan 7. doi: 10.1055/a-1347-6070.

Findings: In a retrospective observational study, 2,574 unselected patients hospitalised in 30 clinical centres in Italy from February 19, 2020 to May 23, 2020 with laboratory-confirmed SARS-CoV-2 infection, were analysed. Out of 2,574 COVID-19 patients, 70.1% received heparin. LMWH was largely the most used formulation (99.5%). Death rates for patients receiving heparin or not were 7.4 and 14.0 per 1,000 person-days, respectively. After adjustment for propensity scores, we found a 40% lower risk of death in patients receiving heparin. This association was particularly evident in patients with a higher severity of disease or strong coagulation activation. In-hospital heparin treatment was associated with lower mortality, particularly in severely ill COVID-19 patients and in those with strong coagulation activation. The results from randomised clinical trials are eagerly awaited to provide clear-cut recommendations.



37. **Safety and Outcomes of Prolonged Usual Care Prone Position Mechanical Ventilation to Treat Acute Coronavirus Disease 2019 Hypoxemic Respiratory Failure.** Douglas IS, Swanson DD, Hiller T, et al. *Crit Care Med.* 2021 Jan 7; doi:10.1097/CCM.0000000000004818.

[https://journals.lww.com/ccmjournal/Abstract/9000/Safety\\_and\\_Outcomes\\_of\\_Prolonged\\_Usual\\_Care\\_Prone.95389.aspx](https://journals.lww.com/ccmjournal/Abstract/9000/Safety_and_Outcomes_of_Prolonged_Usual_Care_Prone.95389.aspx)

Findings: Prolonged prone position ventilation was feasible and relatively safe with implications for wider adoption in treating critically ill coronavirus disease 2019 patients and acute respiratory distress syndrome of other etiologies.

38. **Continuation versus discontinuation of renin-angiotensin system inhibitors in patients admitted to hospital with COVID-19: a prospective, randomised, open-label trial.** Cohen JB, Hanff TC, William P, et al. *Lancet Respir Med.* 2021 Jan 7:S2213-2600(20)30558-0. doi: 10.1016/S2213-2600(20)30558-0.

[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30558-0/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30558-0/fulltext)

FINDINGS: Between March 31 and Aug 20, 2020, 152 participants were enrolled and randomly assigned to either continue or discontinue renin-angiotensin system inhibitor therapy (continuation group n=75; discontinuation group n=77). Mean age of participants was 62 years, 68 (45%) were female, mean body-mass index was 33 kg/m<sup>2</sup> (SD 8), and 79 (52%) had diabetes. Compared with discontinuation of renin-angiotensin system inhibitors, continuation had no effect on the global rank score. There were 16 (21%) of 75 participants in the continuation arm versus 14 (18%) of 77 in the discontinuation arm who required intensive care unit admission or invasive mechanical ventilation, and 11 (15%) of 75 participants in the continuation group versus ten (13%) of 77 in the discontinuation group died. 29 (39%) participants in the continuation group and 28 (36%) participants in the discontinuation group had at least one adverse event ( $\chi^2$  test of adverse events between treatment groups p=0.77). There was no difference in blood pressure, serum potassium, or creatinine during follow-up across the two groups. Consistent with international society recommendations, renin-angiotensin system inhibitors can be safely continued in patients admitted to hospital with COVID-19.

39. **Venovenous extracorporeal membrane oxygenation for patients with refractory coronavirus disease 2019 (COVID-19): Multicenter experience of referral hospitals in a large health care system.** Shih E, DiMaio JM, Squiers JJ, et al. *J Thorac Cardiovasc Surg.* 2020 Dec 1:S0022-5223(20)33145-7. doi: 10.1016/j.jtcvs.2020.11.073. [https://www.jtcvs.org/article/S0022-5223\(20\)33145-7/fulltext](https://www.jtcvs.org/article/S0022-5223(20)33145-7/fulltext)

Findings: We reviewed the clinical course of 37 patients with laboratory-confirmed severe acute respiratory syndrome coronavirus 2 infection supported by venovenous ECMO at 4 ECMO referral centers within a large health care system. The patients had median age of 51 years, and 73% were male. Peak plateau pressures, vasopressor requirements, and arterial partial pressure of carbon dioxide all improved with ECMO support. In our patient population, 24 of 37 patients (64.8%) survived to decannulation and 21 of 37 patients (56.8%) survived to discharge. Among patients discharged alive from the ECMO facility, 12 patients were discharged to a long-term acute care or rehabilitation facility, 2 were transferred back to the referring hospital for ventilatory weaning, and 7 were discharged directly home. For patients who were successfully decannulated, median length of time on ECMO was 17 days. Venovenous ECMO represents a

useful therapy for patients with refractory severe acute respiratory distress syndrome from coronavirus disease 2019.

40. **Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis.** Langford BJ, So M, Raybardhan S, et al. *Clin Microbiol Infect.* 2021 Jan 5:S1198-743X(20)30778-3. doi: 10.1016/j.cmi.2020.12.018. [https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(20\)30778-3/fulltext](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30778-3/fulltext)

Findings: We screened 7469 studies, from which 154 were included in the final analysis. Antibiotic data were available from 30,623 patients. The prevalence of antibiotic prescribing was 74.6%. On univariable meta-regression, antibiotic prescribing was lower in children compared to adults. Antibiotic prescribing was higher with increasing patient age and higher with increasing proportion of patients requiring mechanical ventilation. Estimated bacterial co-infection was 8.6% from 31 studies. Three-quarters of patients with COVID-19 receive antibiotics, prescribing is significantly higher than the estimated prevalence of bacterial co-infection. Unnecessary antibiotic use is likely high in patients with COVID-19.

41. **Open versus percutaneous tracheostomy in COVID-19: a multicentre comparison and recommendation for future resource utilisation.** Rovira A, Tricklebank S, Surda P, et al. *Eur Arch Otorhinolaryngol.* 2021 Jan 9. doi: 10.1007/s00405-020-06597-1. <https://link.springer.com/article/10.1007/s00405-020-06597-1>

Findings: In patients with COVID-19 pneumonitis that require tracheostomy to facilitate weaning from mechanical ventilation, there was no difference in outcomes between those patients that had percutaneous dilatational tracheostomy compared with those that had surgical tracheostomy. Planning for future surges in COVID-19-related critical care demands should utilise all available resource and expertise.

42. **Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19 – Preliminary report.** The REMAP-CAP Investigators, et al. *medRxiv* PREPRINT. 2021.01.07.21249390; doi: <https://doi.org/10.1101/2021.01.07.21249390>  
<https://www.medrxiv.org/content/10.1101/2021.01.07.21249390v1>

Findings: We evaluated tocilizumab and sarilumab in an ongoing international, multifactorial, adaptive platform trial. Adult patients with Covid-19, within 24 hours of commencing organ support in an intensive care unit, were randomized to receive either tocilizumab (8mg/kg) or sarilumab (400mg) or standard care (control). The primary outcome was an ordinal scale combining in-hospital mortality (assigned -1) and days free of organ support to day 21. The trial uses a Bayesian statistical model with pre-defined triggers to declare superiority, efficacy, equivalence or futility. Tocilizumab and sarilumab both met the pre-defined triggers for efficacy. At the time of full analysis 353 patients had been assigned to tocilizumab, 48 to sarilumab and 402 to control. Median organ support-free days were 10 (interquartile range [IQR] -1, 16), 11 (IQR 0, 16) and 0 (IQR -1, 15) for tocilizumab, sarilumab and control, respectively. Relative to control, median adjusted odds ratios were 1.64 (95% credible intervals [CrI] 1.25, 2.14) for tocilizumab and 1.76 (95%CrI 1.17, 2.91) for sarilumab, yielding >99.9% and 99.5% posterior probabilities of superiority compared with control. Hospital mortality was 28.0% (98/350) for tocilizumab, 22.2% (10/45) for sarilumab and 35.8% (142/397) for control.

All secondary outcomes and analyses supported efficacy of these IL-6 receptor antagonists. Conclusions: In critically ill patients with Covid-19 receiving organ support in intensive care, treatment with the IL-6 receptor antagonists, tocilizumab and sarilumab, improved outcome, including survival.

### Transmission / Infection Control

43. **SARS-CoV-2 Transmission from People without COVID-19 Symptoms.** Johansson MA, Quandelacy TM, Kada S, et al. *JAMA Netw Open.* 2021;4(1):e2035057. doi:10.1001/jamanetworkopen.2020.35057 <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2774707?resultClick=3>  
Findings: In this decision analytical model of multiple scenarios of proportions of asymptomatic individuals with COVID-19 and infectious periods, transmission from asymptomatic individuals was estimated to account for more than half of all transmissions. In addition to identification and isolation of persons with symptomatic COVID-19, effective control of spread will require reducing the risk of transmission from people with infection who do not have symptoms. These findings suggest that measures such as wearing masks, hand hygiene, social distancing, and strategic testing of people who are not ill will be foundational to slowing the spread of COVID-19 until safe and effective vaccines are available and widely used.
44. **Confirmed Reinfection with SARS-CoV-2 Variant VOC-202012/01.** Harrington D, Kele B, Pereira S, et al. *Clin Infect Dis.* 2021 Jan 9:ciab014. doi: 10.1093/cid/ciab014. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab014/6076528>  
We have detected a confirmed case of reinfection with SARS-CoV-2 with the second episode due to the 'new variant' VOC-202012/01 of lineage B.1.1.7. The initial infection occurred in the first wave of the pandemic in the UK and was a mild illness. 8 months later, during the second wave of the pandemic in the UK reinfection with the 'new variant' VOC-202012/01 was confirmed and caused a critical illness.
45. **Prevalence and Clinical Significance of Persistent Viral Shedding in Hospitalized Adult Patients with SARS-CoV-2 Infection: A Prospective Observational Study.** Vena A, Taramasso L, Di Biagio A, et al. *Infect Dis Ther.* 2021 Jan 8:1-12. doi: 10.1007/s40121-020-00381-8. <https://link.springer.com/article/10.1007/s40121-020-00381-8>  
Findings: Data were obtained regarding 121 consecutive hospitalized patients with SARS-CoV-2 infection (median age 66 years, male sex 65.3%). Overall, the prevalence of PVS was 38% (46/121 patients). According to univariate analysis, factors associated with PVS were immunosuppression (6.7% vs 21.7%,  $p = 0.02$ ), increased interleukin-6 (IL-6) levels ( $\geq 35$  ng/ml) at the time of diagnosis (43.4% vs 67.3%,  $p = 0.02$ ), time from onset of symptoms to diagnosis (median days 7.0 vs 3.5,  $p = 0.001$ ), intensive care unit admission (22.7% vs 43.5%,  $p = 0.02$ ), and need for invasive mechanical ventilation (20.0% vs 41.3%,  $p = 0.01$ ). PVS was detected in up to 38% of hospitalized patients with SARS-CoV-2 infection and was strongly associated with immunosuppression, increased IL-6 levels, and the need for mechanical ventilation.

46. **Surveillance Testing Reveals a Significant Proportion of Hospitalized Patients with SARS-CoV-2 are Asymptomatic.** Arnold FW, Bishop S, Oppy L, Scott L, Stevenson G. *Am J Infect Control*. 2021 Jan 8;S0196-6553(21)00005-5. doi: 10.1016/j.ajic.2021.01.005.

[https://www.ajicjournal.org/article/S0196-6553\(21\)00005-5/fulltext](https://www.ajicjournal.org/article/S0196-6553(21)00005-5/fulltext)

Findings: Universal surveillance testing for SARS-CoV-2 was performed on patients admitted to this hospital over a 12-week period from April 9, 2020 to July 1, 2020. Positive patients were categorized as either symptomatic or asymptomatic as defined by the 11 criteria per the Centers for Disease Control and Prevention. The positivity rate, proportion with and without symptoms, reasons for admission and geographic distribution in the region were recorded. The positivity rate ranged from 0.8%-6.2%. The proportion of asymptomatic patients with SARS-CoV-2 was 37%. Asymptomatic patients primarily presented to the hospital because of either trauma or labor. Some clusters in the region were identified of both symptomatic and asymptomatic patients. The proportion of asymptomatic patients admitted with SARS-CoV-2 was significant. Identifying and isolating asymptomatic patients likely prevented exposure and development of hospital-acquired COVID-19 cases among healthcare workers and other patients, supporting the universal surveillance of all admitted patients.

## Vaccine

47. **Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine — United States, December 14–23, 2020.** *MMWR Morb Mortal Wkly Rep*. ePub: 6 January 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7002e1>

<https://www.cdc.gov/mmwr/volumes/70/wr/mm7002e1.htm>

Findings: During December 14–23, 2020, monitoring by the Vaccine Adverse Event Reporting System detected 21 cases of anaphylaxis after administration of a reported 1,893,360 first doses of the Pfizer-BioNTech COVID-19 vaccine (11.1 cases per million doses); 71% of these occurred within 15 minutes of vaccination. Locations administering COVID-19 vaccines should adhere to CDC guidance for use of COVID-19 vaccines, including screening recipients for contraindications and precautions, having the necessary supplies available to manage anaphylaxis, implementing the recommended postvaccination observation periods, and immediately treating suspected cases of anaphylaxis with intramuscular injection of epinephrine.

48. **Neutralization of N501Y mutant SARS-CoV-2 by BNT162b2 vaccine-elicited sera.** Xie X, Zou J, Fontes-Garfias CR, et al. *bioRxiv PREPRINT*. Jan 7, 2021. doi:

<https://doi.org/10.1101/2021.01.07.425740>

Findings: Rapidly spreading variants of SARS-CoV-2 that have arisen in the United Kingdom and South Africa share the spike N501Y substitution, which is of particular concern because it is located in the viral receptor binding site for cell entry and increases binding to the receptor (angiotensin converting enzyme 2). We generated isogenic N501 and Y501 SARS-CoV-2. Sera of 20 participants in a previously reported trial of the mRNA-based COVID-19 vaccine BNT162b2 had equivalent neutralizing titers to the N501 and Y501 viruses, evidence the Pfizer-BioNTech vaccine should be effective against these new SARS-CoV-2 variants.

49. **Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection.** Dan JM, Mateus J, Kato Y, et al. *Science*. 2021 Jan 6:eabf4063. doi: 10.1126/science.abf4063. <https://science.sciencemag.org/content/early/2021/01/06/science.abf4063>

Findings: Understanding immune memory to SARS-CoV-2 is critical for improving diagnostics and vaccines, and for assessing the likely future course of the COVID-19 pandemic. We analyzed multiple compartments of circulating immune memory to SARS-CoV-2 in 254 samples from 188 COVID-19 cases, including 43 samples at  $\geq 6$  months post-infection. IgG to the Spike protein was relatively stable over 6+ months. Spike-specific memory B cells were more abundant at 6 months than at 1 month post symptom onset. SARS-CoV-2-specific CD4+ T cells and CD8+ T cells declined with a half-life of 3-5 months. By studying antibody, memory B cell, CD4+ T cell, and CD8+ T cell memory to SARS-CoV-2 in an integrated manner, we observed that each component of SARS-CoV-2 immune memory exhibited distinct kinetics.

### Women & Children

50. **COVID-19 pediatric patients: Gastrointestinal symptoms, presentations, and disparities by race/ethnicity in a large, multi-center United States study.** Ashktorab Y, Brim A, Pizuorno A, Gayam V, Nikdel S, Brim H. *Gastroenterology*. 2021 Jan 6:S0016-5085(21)00028-7. doi: 10.1053/j.gastro.2020.12.078.

<https://www.sciencedirect.com/science/article/pii/S0016508521000287>

Findings: In this study, we describe clinical manifestations of hospitalized COVID-19 US children. The median age in our cohort was 15 years. Most children appear to have mild disease and recover with supportive treatment. There were slightly more males in our cohort. However, it is not unlikely that gender has an impact on outcome. Clinical presentations in children in our cohorts were largely non-specific with predominance of fever and cough among both genders. With respect to GI symptoms, vomiting was the most prevalent symptom. This matches with other reports from Bolia et al. in which they report that the most prevalent GI symptom for children is vomiting. Worth noting, however, that in our small African American patients' group from Interfaith Medical Center, diarrhea, nausea and abdominal pain were represented at 66.6% (2 out of 3 patients), pointing probably at higher GI manifestations in this minority group. Overall, Hispanic and African American children had higher cumulative rates of COVID-19-associated hospitalizations (16.4 and 10.5 per 100,000, respectively) than White children (2.1 per 100,000) and accounted for two thirds of the registered deaths so far.

51. **Trends in Pediatric Hospitalizations for Coronavirus Disease 2019.** Levin Z, Choyke K, Georgiou A, Sen S, Karaca-Mandic P. *JAMA Pediatr*. 2021 Jan 11. doi: 10.1001/jamapediatrics.2020.5535. <https://jamanetwork.com/journals/jamapediatrics/fullarticle/2775008>

Findings: Pediatric hospitalization rates for COVID-19 exhibit significant variation across states and over the course of the pandemic. When ordering the 20 states observed at the end of the study period, most ranked similarly for adult and pediatric hospitalization rates, with some notable exceptions: New Jersey ranked highest for adult hospitalizations in the sample by November 15 but only seventh highest for pediatric hospitalizations. Indiana also had a significant difference, ranking sixth highest for adult hospitalizations but only thirteenth highest for pediatrics. Similarly, Colorado was thirteenth highest for adult but sixth highest for pediatric

hospitalizations. Our results present concerning trends in pediatric hospitalizations. Adult, and especially geriatric, incidence of COVID-19 continues to dominate the national picture, but pediatric populations may require resources that are not readily available across the country.

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## GUIDELINES & CONSENSUS STATEMENTS

[Covid-19 FAQ's in Paediatric and Congenital Cardiology - AEPC position paper](#). Sendzikaite S, Heying R, Milanesi O, Hanseus K, Michel-Behnke I. *Cardiol Young*. 2021 Jan 7:1-21. doi: 10.1017/S1047951120005028.

[Critical observations on and suggested ways forward for healthcare communication during COVID-19: pEACH position paper](#). White SJ, Barello S, Cao di San Marco E, et al. *Patient Educ Couns*. 2020 Dec 26:S0738-3991(20)30689-3. doi: 10.1016/j.pec.2020.12.025.

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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 Vaccine is Limited, Who Should Get Vaccinated First?](#) Updated Jan 8, 2020 to reflect overlap between phases of vaccination priority groups

CDC - [US COVID-19 Cases Caused by Variants](#)

FDA - [Genetic Variants of SARS-CoV-2 May Lead to False Negative Results with Molecular Tests for Detection of SARS-CoV-2 - Letter to Clinical Laboratory Staff and Health Care Providers](#)

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## Commentary & News

[A 7-Point Action Agenda to End the COVID-19 Pandemic for President-elect Biden](#). *JAMA*. 2021 Jan 5;325(1):17-18. doi: 10.1001/jama.2020.23848.

[Covid-19 vaccination: What's the evidence for extending the dosing interval?](#) *BMJ*. 2021 Jan 6;372:n18. doi: 10.1136/bmj.n18.

[Assessing Candidacy for Tracheostomy in Ventilated Patients With Coronavirus Disease 2019: Aligning Patient-Centered Care, Stakeholder Engagement, and Health-Care Worker Safety](#). *Chest*. 2021 Jan;159(1):454-455. doi: 10.1016/j.chest.2020.07.100.

[AN IN VITRO STUDY SHOWS PFIZER-BIONTECH COVID-19 VACCINE ELICITS ANTIBODIES THAT NEUTRALIZE SARS-COV-2 WITH A MUTATION ASSOCIATED WITH RAPID TRANSMISSION](#)

[Why Is Antibiotic Treatment Rarely Performed in COVID-19-Positive Children Admitted in Pediatric Intensive Care Units?](#) *JAMA Pediatr*. 2021 Jan 11. doi: 10.1001/jamapediatrics.2020.5348.



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