COVID-19 Resource Desk

#24 | 9.30.2020 to 10.6.2020

Prepared by System Library Services   Retraction Watch

New Research

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

COVID-19 related publications by Providence caregivers – see Digital Commons

Clinical Syndrome

1. **Retinal findings in patients with COVID-19: Results from the SERPICO-19 study.** Invernizzi A, Torre A, Parrulli S, et al. *EClinicalMedicine.* 2020 Sep 20:100550. doi: 10.1016/j.eclinm.2020.100550. https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30294-7/fulltext
FINDINGS: 54 patients and 133 unexposed subjects were enrolled. Retinal findings in COVID-19 included: haemorrhages (9·25%), cotton wools spots (7·4%), dilated veins (27·7%), tortuous vessels (12·9%). COVID-19 can affect the retina. Retinal veins diameter seems directly correlated with the disease severity. Its assessment could have possible applications in the management of COVID-19.

2. **COVID-19 and Heart Failure with Preserved Ejection Fraction.** Freaney PM, Shah SJ, Khan SS. *JAMA.* 2020 Sep 30. doi: 10.1001/jama.2020.17445.
https://jamanetwork.com/journals/jama/fullarticle/2771385
Findings: Patients with preexisting cardiovascular disease who develop COVID-19 have worse outcomes than patients without CVD. Infection with SARS-CoV-2 can directly or indirectly lead to myocardial injury. Although fulminant viral myocarditis due to COVID-19 appears to be uncommon, recent data, although limited, suggest that direct myocardial injury may occur in some individuals.

3. **In-hospital cardiac arrest in critically ill patients with covid-19: multicenter cohort study.** Hayek SS, Brenner SK, Azam TU, et al. *BMJ.* 2020 Sep 30;371:m3513. doi: 10.1136/bmj.m3513.
https://www.bmj.com/content/371/bmj.m3513
Findings: Among 5019 critically ill patients with covid-19, 14.0% had in-hospital cardiac arrest, 57.1% of whom received cardiopulmonary resuscitation. Patients who had in-hospital cardiac arrest were older (mean age 63), had more comorbidities, and were more likely to be admitted to a hospital with a smaller number of intensive care unit beds compared with those who did not have in-hospital cardiac arrest. Patients who received cardiopulmonary resuscitation were younger than those who did not (mean age 61). The most common rhythms at the time of cardiopulmonary resuscitation were pulseless electrical activity (49.8%, 199/400) and asystole

(23.8%, 95/400). 48 of the 400 patients (12.0%) who received cardiopulmonary resuscitation survived to hospital discharge, and only 7.0% (28/400) survived to hospital discharge with normal or mildly impaired neurological status. Survival to hospital discharge differed by age, with 21.2% of patients younger than 45 years surviving compared with 2.9% of those aged 80 or older. Cardiac arrest is common in critically ill patients with covid-19 and is associated with poor survival, particularly among older patients.

4. **Digestive Manifestations in Patients Hospitalized with COVID-19.** Elmunzer BJ et al. *Clin Gastroenterol Hepatol.* 2020 Sep 30:S1542-3565(20)31371-9. doi: 10.1016/j.cgh.2020.09.041.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7527302/
FINDINGS: A total of 1992 patients across 36 centers met eligibility criteria and were included. Overall, 53% of patients experienced at least one gastrointestinal symptom at any time during their illness, most commonly diarrhea (34%), nausea (27%), vomiting (16%), and abdominal pain (11%). In 74% of cases, gastrointestinal symptoms were judged to be mild. In total, 35% of patients developed an abnormal alanine aminotransferase or total bilirubin level; these were elevated to less than 5 times the upper limit of normal in 77% of cases. After adjusting for potential confounders, the presence of gastrointestinal symptoms at any time or liver test abnormalities on admission were not independently associated with mechanical ventilation or death. Among patients hospitalized with COVID-19, gastrointestinal symptoms and liver test abnormalities were common but the majority were mild and their presence was not associated with a more severe clinical course.

5. **Clinical Characteristics, Hospitalization and Mortality Rates of COVID-19 Among Liver Transplant Patients in the United States: A Multi-Center Research Network Study.** Mansoor E, Perez A, Abou-Saleh M, et al. *Gastroenterology*. 2020 Sep 30:S0016-5085(20)35214-8. doi: 10.1053/j.gastro.2020.09.033.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7525348/pdf/main.pdf
Findings: Liver transplant patients represent one of the largest immunosuppressed cohorts. However, outcomes of COVID-19 in this population remain poorly defined although liver injury has been reported in patients with COVID-19. We found LT patients with COVID-19 to have significantly higher risk of hospitalization, but not a higher risk of mortality, thrombosis or ICU requirement compared to patients without LT and COVID-19 upon adjusted analyses.

Diagnostics & Screening

6. **Comparative study of four SARS-CoV-2 Nucleic Acid Amplification Test (NAAT) platforms demonstrates that ID NOW performance is impaired substantially by patient and specimen type.** Lephart PR, Bachman MA, LeBar W, et al. *Diagn Microbiol Infect Dis*. 2020 Sep 3;99(1):115200. doi: 10.1016/j.diagmicrobio.2020.115200.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7470790/
Findings: We compared the performance of four of these assays that were evaluated for use at our institution: Abbott RealTime m2000 SARS-CoV-2 Assay, DiaSorin Simplexa COVID-19 Direct, Cepheid Xpert Xpress SARS-CoV-2, and Abbott ID NOW COVID-19. Nasopharyngeal and nasal specimens were collected from 88 ED and hospital-admitted patients and tested by the four

methods in parallel to compare performance. ID NOW performance stood out as significantly worse than the other 3 assays despite demonstrating comparable analytic sensitivity. Further study determined that the use of a nasal swab compared to a nylon flocked nasopharyngeal swab, as well as use in a population chronically vs. acutely positive for SARS-CoV-2, were substantial factors.

Epidemiology & Public Health

7. **Changes in Adult Alcohol Use and Consequences During the COVID-19 Pandemic in the US.**
Pollard MS, Tucker JS, Green HD. *JAMA Netw Open.* 2020;3(9):e2022942.
doi:10.1001/jamanetworkopen.2020.22942
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770975
Findings: In this survey study, data were collected using the RAND Corporation American Life Panel (ALP), a nationally representative, probability-sampled panel of 6000 participants age 18 years or more who speak English or Spanish; data are weighted to match a range of national demographic characteristics. A sample of 2615 ALP members ages 30 to 80 years was invited to participate in the baseline survey (wave 1), which was closed after 6 weeks (April 29-June 9, 2019) with 1771 completions. Wave 2 data were collected from May 28 to June 16, 2020, several months after widespread implementation of COVID-19–associated social distancing. The current analytic sample includes 1540 adults from the baseline survey who, approximately 1 year later, completed the wave 2 survey. Frequency of alcohol consumption increased overall, 0.74 days, representing an increase of 14% over the baseline of 5.48 days in 2019. On average, alcohol was consumed 1 day more per month by 3 of 4 adults.

8. **Recent Increase in COVID-19 Cases Reported Among Adults Aged 18–22 Years — United States, May 31–September 5, 2020.** Salvatore PP, Sula E, Coyle JP, et al. *MMWR Morb Mortal Wkly Rep.* ePub: 29 September 2020. DOI:
http://dx.doi.org/10.15585/mmwr.mm6939e4external icon
https://www.cdc.gov/mmwr/volumes/69/wr/mm6939e4.htm
Findings: During August 2–September 5, 2020, weekly COVID-19 cases among persons aged 18–22 years increased 55% nationally. Increases were greatest in the Northeast (144%) and Midwest (123%). Increases in cases were not solely attributable to increased testing. Young adults, including those enrolled in colleges and universities, should take precautions, including mask wearing, social distancing, and hand hygiene, and follow local, state, and federal guidance for minimizing the spread of COVID-19. Institutions of higher education should take action to promote healthy environments.

9. **Changing Age Distribution of the COVID-19 Pandemic - United States, May-August 2020.**
Boehmer TK, DeVies J, Caruso E, et al. *MMWR Morb Mortal Wkly Rep.* 2020 Oct 2;69(39):1404-1409. doi: 10.15585/mmwr.mm6939e1.
https://www.cdc.gov/mmwr/volumes/69/wr/mm6939e1.htm
Findings: Nationwide, the median age of COVID-19 cases declined from 46 years in May to 37 years in July and 38 in August. Similar patterns were seen for COVID-19-like illness-related ED visits and positive SARS-CoV-2 RT-PCR test results in all U.S. Census regions. During June-

August, COVID-19 incidence was highest in persons aged 20-29 years, who accounted for >20% of all confirmed cases. The southern United States experienced regional outbreaks of COVID-19 in June. In these regions, increases in the percentage of positive SARS-CoV-2 test results among adults aged 20-39 years preceded increases among adults aged ≥60 years by an average of 8.7 days, suggesting that younger adults likely contributed to community transmission of COVID-19. Given the role of asymptomatic and presymptomatic transmission, strict adherence to community mitigation strategies and personal preventive behaviors by younger adults is needed to help reduce their risk for infection and subsequent transmission of SARS-CoV-2 to persons at higher risk for severe illness.

10. **Case Series of Multisystem Inflammatory Syndrome in Adults Associated with SARS-CoV-2 Infection — United Kingdom and United States, March–August 2020.** Morris SB, Schwartz NG, Patel P, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 2 October 2020. DOI: http://dx.doi.org/10.15585/mmwr.mm6940e1
    Findings: Cases reported to CDC and published case reports and series identify MIS-A in adults, who usually require intensive care and can have fatal outcomes. Antibody testing was required to identify SARS-CoV-2 infection in approximately one third of 27 cases. Clinical suspicion and indicated SARS-CoV-2 testing, including antibody testing, might be needed to recognize and treat adults with MIS-A. Further research is needed to understand the pathogenesis and long-term effects of this condition. Ultimately, the recognition of MIS-A reinforces the need for prevention efforts to limit spread of SARS-CoV-2.

Healthcare Delivery & Healthcare Workers

11. **Efficacy and Safety of Hydroxychloroquine vs Placebo for Pre-exposure SARS-CoV-2 Prophylaxis among Health Care Workers: A Randomized Clinical Trial.** Abella BS, Jolkovsky EL, Biney BT, et al. *JAMA Intern Med*. September 30, 2020. doi:10.1001/jamainternmed.2020.6319
    https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2771265
    Findings: In this double-blind, placebo-controlled randomized clinical trial that included 132 participants and was terminated early, there was not a significant difference in reverse-transcriptase polymerase chain reaction–confirmed SARS-CoV-2 incidence between hydroxychloroquine and placebo cohorts. Among hospital-based health care workers, daily hydroxychloroquine did not prevent SARS-CoV-2 infection, although the trial was terminated early and may have been underpowered to detect a clinically important difference.

12. **Impact of the COVID-19 pandemic on clinical research.** Katherine R Tuttle **[PSJH author]**. *Nat Rev Nephrol.* 2020 Oct;16(10):562-564. doi: 10.1038/s41581-020-00336-9.
    https://www.nature.com/articles/s41581-020-00336-9
    The COVID-19 pandemic has placed a tremendous strain on sustaining the clinical research enterprise and will also likely affect key study outcomes; these effects must be considered during data analysis and interpretation. Nevertheless, the responses to the pandemic have also introduced innovations that will advance the conduct of clinical research.

13. **Use and Content of Primary Care Office-Based vs Telemedicine Care Visits during the COVID-19 Pandemic in the US.** Alexander GC, Tajanlangit M, Heyward J, et al. *JAMA Netw Open*. 2020 Oct 1;3(10):e2021476. doi: 10.1001/jamanetworkopen.2020.21476.
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2771191
Findings: Between January 1, 2018, and December 31, 2019, an average of 125.8 million quarterly primary care visits occurred in the US, most of which were office-based (92.9%). In 2020, the total number of encounters decreased to 117.9 million in Q1 and 99.3 million in Q2, a decrease of 21.4% (27.0 million visits) from the average of Q2 levels during 2018 and 2019. Office-based visits decreased 50.2% (59.1 million visits) in Q2 of 2020 compared with Q2 2018-2019, while telemedicine visits increased from 1.1% of total Q2 2018-2019 visits (1.4 million quarterly visits) to 4.1% in Q1 of 2020 (4.8 million visits) and 35.3% in Q2 of 2020 (35.0 million visits). Decreases occurred in blood pressure level assessment (50.1% decrease, 44.4 million visits) and cholesterol level assessment (36.9% decrease, 10.2 million visits) in Q2 of 2020 compared with Q2 2018-2019 levels. New medication visits in Q2 of 2020 decreased by 26.0% (14.1 million visits) from Q2 2018-2019 levels. Telemedicine adoption occurred at similar rates among White individuals and Black individuals (19.3% vs 20.5% of patient visits, respectively, in Q1/Q2 of 2020), varied by region (low of 15.1% of visits [East North Central region], high of 26.8% of visits [Pacific region]), and was not correlated with regional COVID-19 burden. The COVID-19 pandemic has been associated with changes in the structure of primary care delivery, with the content of telemedicine visits differing from that of office-based encounters.

Laboratory Results

14. **Waning of SARS-CoV-2 RBD antibodies in longitudinal convalescent plasma samples within four months after symptom onset.** Perreault J, Tremblay T, Fournier M, et al. *Blood.* 2020 Oct 1;blood.2020008367. doi: 10.1182/blood.2020008367.
https://ashpublications.org/blood/article/doi/10.1182/blood.2020008367/463996/Waning-of-SARS-CoV-2-RBD-antibodies-in
Findings: The study included 15 adults who recovered from COVID-19. Their symptoms ranged from mild to severe, but none were hospitalized. Each person donated plasma between four and nine times. The first donation was 33 to 77 days after symptoms began, and the last donation was made between 66 and 114 days. By about 88 days, all 15 donors had decreases in antibodies, and half of detectable antibodies dropped within 21 days after that, the investigators found. Based on these findings, she said clinicians should check for presence of antibodies before giving donor plasma to a patient.

15. **Prolonged presence of viral nucleic acid in clinically recovered COVID-19 patients was not associated with effective infectiousness.** Hong K, Cao W, Liu Z, et al. *Emerg Microbes Infect.* 2020 Sep 28:1-26. doi: 10.1080/22221751.2020.1827983.
https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1827983
Findings: Prolonged presence of viral nucleic acid was reported in certain patients with COVID-19, with unclear clinical and epidemiological significance. We here described the clinical and epidemiological characteristics of 37 recovered COVID 19 patients with prolonged presence of viral RNA in Wuhan, China. For those who had been discharged and re-admitted, their close

contacts outside the hospital were traced and evaluated. The median age of the 37 patients was 62 years, and 24 (64.9%) were men. They had common or severe COVID-19. With prolonged positive RT-PCR, most patients were clinically stable, 29 (78.4%) denied any symptoms. A total of 431 PCR tests were carried out, with each patient at a median of 8 time points. The median time of PCR positivity to April 18 was 78 days, and the longest 120 days. 22 of 37 patients had been discharged at a median of 44 days from disease onset, and 9 had lived with their families without personal protections for a total of 258 person-days and no secondary infection was identified through epidemiological investigation, nucleic acid and antibody screening. Infectiousness in COVID-19 patients with prolonged presence of viral nucleic acid should not solely be evaluated by RT-PCR. Those patients who have clinically recovered and whose disease course has exceeded four weeks were associated with very limited infectiousness. Reconsideration of disease control in such patients is needed.

16. **Dynamics of neutralizing antibody titers in the months after SARS-CoV-2 infection.** Crawford KHD, Dingens AS, Eguia R, et al. *J Infect Dis.* 2020 Sep 30:jiaa618. doi: 10.1093/infdis/jiaa618. https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa618/5916372?searchresult=1
Findings: Here we quantify how levels of these antibodies change in the months following SARS-CoV-2 infection by examining longitudinal samples collected between ~30 and 152 days post symptom onset from a prospective cohort of 32 recovered individuals with asymptomatic, mild, or moderate-severe disease. Neutralizing antibody titers declined an average of about four-fold from one to four months post symptom onset. This decline in neutralizing antibody titers was accompanied by a decline in total antibodies capable of binding the viral spike or its receptor-binding domain. Importantly, our data are consistent with the expected early immune response to viral infection, where an initial peak in antibody levels is followed by a decline to a lower plateau. Additional studies of long-lived B-cells and antibody titers over longer time frames are necessary to determine the durability of immunity to SARS-CoV-2.

17. **IL-6 serum levels predict severity and response to Tocilizumab in COVID-19: an observational study.** Galván-Román JM, Rodríguez-García SC, Roy-Vallejo E, et al. *J Allergy Clin Immunol.* 2020 Sep 30:S0091-6749(20)31329-4. doi: 10.1016/j.jaci.2020.09.018. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7525244/
Findings: One hundred and forty-six patients were studied, predominantly male (66%); median age was 63 years. Forty-four patients (30%) required IMV, and 58 patients (40%) received treatment with TCZ. IL-6 levels>30 pg/ml was the best predictor for IMV (OR:7.1; p<0.001). Early administration of TCZ was associated with improvement of oxygenation (PaO2/FiO2) in patients with high IL-6 (p=0.048). Patients with high IL-6 not treated with TCZ showed high mortality (HR: 4.6; p=0.003), as well as those with low IL-6 treated with TCZ (HR: 3.6; p=0.016). No relevant serious adverse events were observed in TCZ-treated patients. Baseline IL-6>30 pg/ml predicts IMV requirement in patients with COVID-19 and contributes to establish an adequate indication for TCZ administration.

18. **Effect of Acid Suppressants on the Risk of COVID-19: A Propensity Score Matched Study using UK Biobank Acid Suppressants and the Risk of COVID-19.** Fan X, Liu Z, Miyata T, et al. *Gastroenterology*. 2020 Sep 24:S0016-5085(20)35209-4. doi: 10.1053/j.gastro.2020.09.028. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7513758/pdf/main.pdf
Findings: Our findings indicated that neither PPI nor H2RA use was associated with the risk of SARS-CoV-2 infection and death in patients with COVID-19. A notable exception was found in patients with upper gastrointestinal diseases taking the omeprazole who were more susceptible to SARS-CoV-2; this was not observed with use of other types of PPIs. In addition, no evidence of increased SARS-CoV-2 susceptibility was found with the use of PPI or H2RA in the meta-analysis.

19. **Risk of COVID-19-related death among patients with chronic obstructive pulmonary disease or asthma prescribed inhaled corticosteroids: an observational cohort study using the OpenSAFELY platform.** Schultze A, Walker AJ, MacKenna B, et al. *Lancet Respir Med*. 2020 Sep 24:S2213-2600(20)30415-X. doi: 10.1016/S2213-2600(20)30415-X. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30415-X/fulltext
FINDINGS: We identified 148 557 people with COPD and 818 490 people with asthma who were given relevant respiratory medications in the 4 months before the index date. People with COPD who were prescribed ICSs were at increased risk of COVID-19-related death compared with those prescribed LABA-LAMA combinations. Compared with those prescribed SABAs only, people with asthma who were prescribed high-dose ICS were at an increased risk of death, whereas those given a low or medium dose were not. Sensitivity analyses showed that the apparent harmful association we observed could be explained by relatively small health differences between people prescribed ICS and those not prescribed ICS that were not recorded in the database. Our results do not support a major role for regular ICS use in protecting against COVID-19-related death among people with asthma or COPD. Observed increased risks of COVID-19-related death can be plausibly explained by unmeasured confounding due to disease severity.

20. **Renin-Angiotensin System Blockers and Adverse Outcomes of Influenza and Pneumonia: A Danish Cohort Study.** Christiansen CF, Heide-Jørgensen U, Rasmussen TB, et al. *J Am Heart Assoc*. 2020 Oct 1:e017297. doi: 10.1161/JAHA.120.017297. https://www.ahajournals.org/doi/10.1161/JAHA.120.017297
Findings: This cohort study included all adult patients hospitalized with influenza or pneumonia from 2005 to 2018 in Denmark using population-based medical databases. Thirty-day mortality and risk of admission to the intensive care unit in ACE-Is/ARBs users was compared with nonusers and with users of calcium channel blockers. In propensity score-weighted analyses, ACE-I/ARB users had marginally lower 30-day mortality than users of calcium channel blockers (13.9% versus 14.5%), and a lower risk of admission to the intensive care unit (8.0% versus 9.6%). Compared with nonusers, current ACE-I/ARB users had lower mortality, but similar risk of admission to the intensive care unit. Conclusions Among patients with influenza or

pneumonia, ACE-I/ARB users had no increased risk of admission to the intensive care unit and slightly reduced mortality after controlling for confounding.

21. **Association of a Prior Psychiatric Diagnosis with Mortality among Hospitalized Patients with Coronavirus Disease 2019 (COVID-19) Infection.** Li L, Li F, Fortunati F, Krystal JH. *JAMA Netw Open*. 2020;3(9):e2023282. doi:10.1001/jamanetworkopen.2020.23282 https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2771037
Findings: Psychiatric disorders are associated with shortened life expectancy (ie, shortened by as much as 10 years). A large population study in Demark suggested that an a priori diagnosis of depression was associated with a higher 30-day mortality for those hospitalized for an infection. Here, we show patients with a prior psychiatric diagnosis while hospitalized for COVID-19 had a higher mortality rate compared those without a psychiatric condition.

22. **Early prediction of disease progression in COVID-19 pneumonia patients with chest CT and clinical characteristics.** Feng Z, Yu Q, Yao S, et al. *Nat Commun*. 2020 Oct 2;11(1):4968. doi: 10.1038/s41467-020-18786-x. https://www.nature.com/articles/s41467-020-18786-x
Findings: We conducted a multicenter retrospective study involving patients with moderate COVID-19 pneumonia to investigate the utility of chest computed tomography (CT) and clinical characteristics to risk-stratify the patients. Our results show that CT severity score is associated with inflammatory levels and that older age, higher neutrophil-to-lymphocyte ratio (NLR), and CT severity score on admission are independent risk factors for short-term progression. The nomogram based on these risk factors shows good calibration and discrimination in the derivation and validation cohorts. These findings have implications for predicting the progression risk of COVID-19 pneumonia patients at the time of admission. CT examination may help risk-stratification and guide the timing of admission.

23. **Outcome of Hospitalization for COVID-19 in Patients with Interstitial Lung Disease: An International Multicenter Study.** Drake TM, Docherty AB, Harrison EM, et al. *Am J Respir Crit Care Med.* 2020 Oct 2. doi: 10.1164/rccm.202007-2794OC.
https://www.atsjournals.org/doi/pdf/10.1164/rccm.202007-2794OC
Findings: Data from 349 patients with ILD across Europe were included, of whom 161 were admitted to hospital with laboratory or clinical evidence of COVID-19 and eligible for propensity-score matching. Overall mortality was 49% (79/161) in patients with ILD with COVID-19. After matching ILD patients with COVID-19 had higher mortality (HR 1.60, Confidence Intervals 1.17-2.18 p=0.003) compared with age, sex and co-morbidity matched controls without ILD. Patients with a Forced Vital Capacity (FVC) of <80% had an increased risk of death versus patients with FVC ≥80% (HR 1.72, 1.05-2.83). Furthermore, obese patients with ILD had an elevated risk of death (HR 2.27, 1.39-3.71). Patients with ILD are at increased risk of death from COVID-19, particularly those with poor lung function and obesity. Stringent precautions should be taken to avoid COVID-19 in patients with ILD.

Survivorship & Rehabilitation

24. **Rehabilitation and COVID-19: the Cochrane Rehabilitation 2020 rapid living systematic review. Update as of August 31st, 2020.** International Multiprofessional Steering Committee of Cochrane Rehabilitation REH-COVER action. *Eur J Phys Rehabil Med.* 2020 Oct 1. doi: 10.23736/S1973-9087.20.06614-9. https://www.minervamedica.it/en/journals/europa-medicophysica/article.php?cod=R33Y9999N00A20100102
Findings: After removing duplicates, 1136 papers were identified, and 51 studies were finally included. According to OCEBM 2011 Levels of Evidence Table, they were Level 4 in most cases (76.5%) and Level 3 in the remaining (23.5%). Randomized controlled trials (RCTs) were not found. Thirty-two studies (62.7%) included COVID-19 patients who were assessed in the acute (20/32) or post-acute phases (12/32). The other studies reported data on the impact of COVID-19 infection (7/19) or on the effect of lockdown restrictions (12/19) on subjects with pre-existing health conditions. The scientific literature of August 2020 mainly focused on limitations in functioning of nervous system structure and related functions. Albeit the increased availability of data from analytical studies (both cohort and cross-sectional), there is still a lack of well-.conductedLevel 2 studies, to improve the knowledge on the effects of rehabilitation in COVID-19 patients.

25. **Long-term Health Consequences of COVID-19.** del Rio C, Collins LF, Malani P. *JAMA.* October 5, 2020. doi:10.1001/jama.2020.19719
https://jamanetwork.com/journals/jama/fullarticle/2771581
Granted that no long-term data of substantial numbers of patients with various presenting symptoms exist and with comparison groups, and that it is still early in the COVID-19 pandemic, it is possible that large numbers of patients will experience long-term sequelae. Outpatient post–COVID-19 clinics are opening in many localities where large outbreaks have occurred, and the term "long-haulers" has been suggested to refer to these patients. It is imperative that the care of this vulnerable patient population take a multidisciplinary approach, with a thoughtfully integrated research agenda, to avoid health system fragmentation and to allow the comprehensive study of long-term health consequences of COVID-19 on multiple organ systems and overall health and well-being. Furthermore, such an approach will provide the opportunity to efficiently and systematically conduct studies of therapeutic interventions to mitigate the adverse physical and mental health effects among hundreds of thousands, if not millions, of people who recover from COVID-19. Longer-ranging longitudinal observational studies and clinical trials will be critical to elucidate the durability and depth of health consequences attributable to COVID-19 and how these may compare with other serious illnesses.

Therapeutics

26. **An open-label, randomized trial of the combination of IFN-κ plus TFF2 with standard care in the treatment of patients with moderate COVID-19.** Fu W, Liu Y, Liu L, et al. *EClinicalMedicine*. 2020 Sep 20:100547. doi: 10.1016/j.eclinm.2020.100547.
https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30291-1/fulltext

Findings: We found that aerosol inhalation of IFN-κ plus TFF2 in combination with standard care is safe and superior to standard care alone in shortening the time up to viral RNA negative conversion in all clinical samples. In addition, the patients in experimental group had a significantly shortened CT imaging improvement time than those in control group. This study suggested that this combination treatment is able to facilitate clinical improvement (negative for virus, improvement by CT, reduced hospitalization stay) and thereby result in an early release from the hospital. These data support the need for exploration with a large-scale trial of IFN-κ plus TFF2 to treat COVID-19.

27. **Factors Associated with Good Patient Outcomes Following Convalescent Plasma in COVID-19: A Prospective Phase II Clinical Trial.** Ibrahim D, Dulipsingh L, Zapatka L, et al. *Infect Dis Ther.* 2020 Sep 20:1-14. doi: 10.1007/s40121-020-00341-2.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7502154/
Findings: Of the 38 patients included in the analysis, 24 (63%) recovered and were discharged, and 14 (37%) died. Patients who received convalescent plasma early in the disease course (severe illness group) as compared to the patients that received convalescent plasma later in the disease progression (critical illness group) had significantly lower hospital mortality 13% vs 55% (p < 0.02) and shorter mean hospital length of stay 15.4 vs 33 days (p < 0.01). One patient experienced a transient transfusion reaction. No other adverse effects of convalescent plasma infusion were observed. Our results suggest that convalescent plasma with adequate anti-SARS-CoV-2 antibody titer is safe and has the potential for positive impact on clinical outcomes including recovery and survival if given to patients early in the course of COVID-19 disease.

28. **Sitagliptin Treatment at the Time of Hospitalization Was Associated with Reduced Mortality in Patients with Type 2 Diabetes and COVID-19: A Multicenter, Case-Control, Retrospective, Observational Study.** Solerte SB, D'Addio F, Trevisan R, et al. *Diabetes Care.* 2020 Sep 29:dc201521. doi: 10.2337/dc20-1521.
https://care.diabetesjournals.org/content/diacare/early/2020/09/22/dc20-1521.full.pdf
Findings: Of the 338 consecutive patients with type 2 diabetes and COVID-19 admitted in Northern Italy hospitals included in this study, 169 were on sitagliptin, while 169 were on standard of care. Treatment with sitagliptin at the time of hospitalization was associated with reduced mortality (18% vs. 37% of deceased patients), with an improvement in clinical outcomes (60% vs. 38% of improved patients) and with a greater number of hospital discharges (120 vs. 89 of discharged patients) compared with patients receiving standard of care, respectively. In this multicenter, case-control, retrospective, observational study of patients with type 2 diabetes admitted to the hospital for COVID-19, sitagliptin treatment at the time of hospitalization was associated with reduced mortality and improved clinical outcomes as compared with standard-of-care treatment. The effects of sitagliptin in patients with type 2 diabetes and COVID-19 should be confirmed in an ongoing randomized, placebo-controlled trial.

29. **Low-to-moderate dose corticosteroids treatment in hospitalized adults with COVID-19.** Liu Z, Li X, Fan G, et al. *Clin Microbiol Infect.* 2020 Sep 29:S1198-743X(20)30599-1. doi:

10.1016/j.cmi.2020.09.045. https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30599-1/fulltext

Findings: Among 646 patients, in-hospital death rate was higher in 158 patients with corticosteroids administration (72/158, 45.6% vs 56/488). After propensity score-match analysis, no significant differences were observed in in-hospital death between patients with and without corticosteroids treatment (47/124, 37.9% vs 47/124, 37.9%). When patients received corticosteroids before they required nasal high-flow oxygen therapy or mechanical ventilation, in-hospital death rate was lower than that in patients who were not administered with corticosteroids (17/86, 19.8% vs. 26/86, 30.2%,), whereas time from admission to clinical improvement was longer (13 days vs 10 days). Corticosteroids use in COVID-19 patients may not be associated with in-hospital mortality.

30. **Lopinavir–ritonavir in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial.** RECOVERY Collaborative Group. *Lancet,* October 5, 2020. https://doi.org/10.1016/ S0140-6736(20)32013-4
https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)32013-4.pdf

Findings: Between March 19, 2020, and June 29, 2020, 1616 patients were randomly allocated to receive lopinavir–ritonavir and 3424 patients to receive usual care. Overall, 374 (23%) patients allocated to lopinavir–ritonavir and 767 (22%) patients allocated to usual care died within 28 days. Results were consistent across all prespecified subgroups of patients. We observed no significant difference in time until discharge alive from hospital (median 11 days in both groups) or the proportion of patients discharged from hospital alive within 28 days. Among patients not on invasive mechanical ventilation at baseline, there was no significant difference in the proportion who met the composite endpoint of invasive mechanical ventilation or death. In patients admitted to hospital with COVID-19, lopinavir–ritonavir was not associated with reductions in 28-day mortality, duration of hospital stay, or risk of progressing to invasive mechanical ventilation or death. These findings do not support the use of lopinavir–ritonavir for treatment of patients admitted to hospital with COVID-19.

Transmission / Infection Control

31. **The role of the healthcare surface environment in SARS-CoV-2 transmission and potential control measures.** Kanamori H, Weber DJ, Rutala WA. *Clin Infect Dis*. 2020 Sep 28:ciaa1467. doi: 10.1093/cid/ciaa1467. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1467/5912347

Findings: We reviewed survival, contamination, and transmission of SARS-CoV-2 via environmental surfaces and shared medical devices as well as environmental disinfection of COVID-19 in healthcare settings. Coronaviruses, including SARS-CoV-2, have been demonstrated to survive for hours to days on environmental surfaces depending on experimental conditions. The healthcare environment is frequently contaminated with SARS-CoV-2 RNA in most studies but without evidence of viable virus. Although direct exposure to respiratory droplets is the main transmission route of SARS-CoV-2, the contaminated healthcare environment can potentially result in transmission of SARS-CoV-2 as described with other coronaviruses such as SARS-CoV and MERS-CoV. It is important to improve thoroughness

of cleaning/disinfection practice in healthcare facilities and select effective disinfectants to decontaminate inanimate surfaces and shared patient care items.

32. **Effect of Face Masks on Gas Exchange in Healthy Persons and Patients with COPD.** Samannan R, Holt G, Calderon-Candelario R, et al. *Ann Am Thorac Soc.* 2020 Oct 2. doi: 10.1513/AnnalsATS.202007-812RL.
https://www.atsjournals.org/doi/pdf/10.1513/AnnalsATS.202007-812RL
Findings: This data find that gas exchange is not significantly affected by the use of surgical mask, even in subjects with severe lung impairment. The discomfort felt with surgical mask use has been ascribed to neurological reactions (increased afferent impulses from the highly thermosensitive area of the face covered by the mask or from the increased temperature of the inspired air) or associated psychological phenomena such as anxiety, claustrophobia or affective responses to perceived difficulty in breathing.

33. **Survival of SARS-CoV-2 and influenza virus on the human skin: Importance of hand hygiene in COVID-19.** Hirose R, Ikegaya H, Naito Y, et al. *Clinical Infectious Diseases.* Oct 3, 2020.
https://doi.org/10.1093/cid/ciaa1517 https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1517/5917611
Findings: SARS-CoV-2 and IAV were inactivated more rapidly on skin surfaces than on other surfaces (stainless steel/glass/plastic); the survival time was significantly longer for SARS-CoV-2 than for IAV 9.04 h vs. 1.82 h. IAV on other surfaces was inactivated faster in mucus versus medium conditions, while SARS-CoV-2 showed similar stability in the mucus and medium; the survival time was significantly longer for SARS-CoV-2 than for IAV [11.09 h vs. 1.69 h]. Moreover, both SARS-CoV-2 and IAV in the mucus/medium on human skin were completely inactivated within 15 s by ethanol treatment. The 9-h survival of SARS-CoV-2 on human skin may increase the risk of contact transmission in comparison with IAV, thus accelerating the pandemic. Proper hand hygiene is important to prevent the spread of SARS-CoV-2 infections.

34. **A quantitative evaluation of aerosol generation during tracheal intubation and extubation.** Brown J, Gregson FKA, Shrimpton A, et al. *Anaesthesia* 2020 Oct 6.
https://doi.org/10.1111/anae.15292 https://associationofanaesthetists-publications.onlinelibrary.wiley.com/doi/10.1111/anae.15292
Findings: We conducted real-time, high-resolution environmental monitoring in ultraclean ventilation operating theatres during tracheal intubation and extubation sequences. Continuous sampling with an optical particle sizer allowed characterisation of aerosol generation within the zone between the patient and anaesthetist. Aerosol monitoring showed a very low background particle count (0.4 particles.l-1) allowing resolution of transient increases in airborne particles associated with airway management. A positive reference control quantitated the aerosol produced in the same setting by a volitional cough (average concentration, 732 (418) particles.l-1, n = 38). Tracheal intubation including face-mask ventilation produced very low quantities of aerosolised particles (average concentration, 1.4 (1.4) particles.l-1, n = 14, p < 0·0001 vs. cough). Tracheal extubation, particularly when the patient coughed, produced a detectable aerosol (21 (18) l-1, n = 10) which was 15-fold greater than intubation (p = 0.0004) but 35-fold less than a volitional cough (p < 0.0001). The study

does not support the designation of elective tracheal intubation as an aerosol-generating procedure. Extubation generates more detectable aerosol than intubation but falls below the current criterion for designation as a high risk aerosol-generating procedure. These novel findings from real-time aerosol detection in a routine healthcare setting provide a quantitative methodology for risk assessment that can be extended to other airway management techniques and clinical settings. They also indicate the need for reappraisal of what constitutes an aerosol-generating procedure and the associated precautions for routine anaesthetic airway management.

Vaccine

35. **US Adults' Preferences for Public Allocation of a Vaccine for Coronavirus Disease 2019.** Gollust SE, Saloner B, Hest R, et al. *JAMA Netw Open*. 2020;3(9):e2023020. doi:10.1001/jamanetworkopen.2020.23020
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770976?resultClick=3
Findings: This survey study found that respondents' preferences were consistent with experts' emergent recommendations for priority populations for vaccination, suggesting the public would support guidelines that offer vaccine priority to groups defined by age, risk of dying, and employment type. More than 90% of respondents identified medical workers as high priority. They also rated people at highest risk of dying as higher priority than people with lower risk.

36. **Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults.** Anderson EJ et al. *NEJM* 2020 Sep 29. DOI: 10.1056/NEJMoa2028436
https://www.nejm.org/doi/full/10.1056/NEJMoa2028436
Findings: Solicited adverse events were predominantly mild or moderate in severity and most frequently included fatigue, chills, headache, myalgia, and pain at the injection site. Such adverse events were dose-dependent and were more common after the second immunization. Binding-antibody responses increased rapidly after the first immunization. By day 57, among the participants who received the 25-μg dose, the anti–S-2P geometric mean titer (GMT) was 323,945 among those between the ages of 56 and 70 years and 1,128,391 among those who were 71 years of age or older; among the participants who received the 100-μg dose, the GMT in the two age subgroups was 1,183,066 and 3,638,522, respectively. After the second immunization, serum neutralizing activity was detected in all the participants by multiple methods. Binding- and neutralizing-antibody responses appeared to be similar to those previously reported among vaccine recipients between the ages of 18 and 55 years and were above the median of a panel of controls who had donated convalescent serum. The vaccine elicited a strong CD4 cytokine response involving type 1 helper T cells. In this small study involving older adults, adverse events associated with the mRNA-1273 vaccine were mainly mild or moderate. The 100-μg dose induced higher binding- and neutralizing-antibody titers than the 25-μg dose, which supports the use of the 100-μg dose in a phase 3 vaccine trial.

37. **Framework for Equitable Allocation of COVID-19 Vaccine.** National Academies of Sciences, Engineering, and Medicine. 2020. Washington, DC: *The National Academies Press*.

https://doi.org/10.17226/25917. https://www.nap.edu/catalog/25917/framework-for-equitable-allocation-of-covid-19-vaccine
In response to the COVID-19 pandemic and the societal disruption it has brought, national governments and the international community have invested billions of dollars and immense amounts of human resources to develop a safe and effective vaccine in an unprecedented time frame. Vaccination against this novel coronavirus, SARS-CoV-2, offers the possibility of significantly reducing severe morbidity and mortality and transmission when deployed alongside other public health strategies and improved therapies. Health equity is intertwined with the impact of COVID-19 and there are certain populations that are at increased risk of severe illness or death from COVID-19. In the United States and worldwide, the pandemic is having a disproportionate impact on people who are already disadvantaged by virtue of their race and ethnicity, age, health status, residence, occupation, socioeconomic condition, or other contributing factors. Framework for Equitable Allocation of COVID-19 Vaccine offers an overarching framework for vaccine allocation to assist policy makers in the domestic and global health communities. Built on widely accepted foundational principles and recognizing the distinctive characteristics of COVID-19, this report's recommendations address the commitments needed to implement equitable allocation policies for COVID-19 vaccine.

Whole Person Care

38. **COVID-19 and Psychological Distress—Changes in Internet Searches for Mental Health Issues in New York During the Pandemic.** Stijelja S, Mishara BL. *JAMA Intern Med*. October 5, 2020. doi:10.1001/jamainternmed.2020.3271
https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2771502?resultClick=1
Findings: Searches for anxiety, panic attack, and insomnia rose significantly during the lockdown, then eventually reverted to their mean. Assuming this is indicative of significant increases in these symptoms, this suggests the need to provide focused competent online and telemedicine services during quarantines. Searches for depression did not increase during the lockdown. However, depression could increase if the quarantines return or as a result of the economic turmoil and unemployment that might ensue. Suicide queries did not increase during the lockdown. This is consistent with reports from the New York City crisis line, NYC Well, which despite a 40% increase in calls during this period, experienced no increase in the number of callers with suicidal ideation and no increase in emergency suicide rescues.

Women & Children

39. **COVID-19 and Parent Intention to Vaccinate Their Children against Influenza.** Sokol RL, Grummon AH. *Pediatrics*. 2020 Sep 30:e2020022871. doi: 10.1542/peds.2020-022871.
https://pediatrics.aappublications.org/content/pediatrics/early/2020/09/28/peds.2020-022871.full.pdf
Findings: Changes in vaccination intentions significantly differed between parents whose children received the 2019-2020 influenza vaccine compared to those whose children did not. Specifically, among parents whose children did not receive the 2019-2020 vaccine, 34% reported that the COVID-19 pandemic made them less likely to have their child receive the

2020-2021 vaccine. Among those whose children did receive the 2019-2020 vaccine, this figure was just 24%. Conversely, only 21% of parents whose children did not receive the 2019-2020 vaccine reported that the COVID-19 pandemic made them more likely to have their child receive the 2020-2021 vaccine, compared to 39% of parents whose children did receive the 2019-2020 vaccine. The COVID-19 pandemic alone does not appear sufficient to encourage the uptake of pediatric seasonal influenza vaccination. Instead, the COVID-19 pandemic may exacerbate polarity in vaccination uptake.

40. **COVID-19 Trends Among School-Aged Children - United States, March 1-September 19, 2020.** Leeb RT, Price S, Sliwa S, et al. *MMWR Morb Mortal Wkly Rep.* 2020 Oct 2;69(39):1410-1415. doi: 10.15585/mmwr.mm6939e2.
https://www.cdc.gov/mmwr/volumes/69/wr/mm6939e2.htm
Findings: During May-September 2020, average weekly incidence (cases per 100,000 children) among adolescents aged 12-17 years (37.4) was approximately twice that of children aged 5-11 years (19.0). In addition, among school-aged children, COVID-19 indicators peaked during July 2020: weekly percentage of positive SARS-CoV-2 test results increased from 10% on May 31 to 14% on July 5; SARS-CoV-2 test volume increased from 100,081 tests on May 31 to 322,227 on July 12, and COVID-19 incidence increased from 13.8 per 100,000 on May 31 to 37.9 on July 19. During July and August, test volume and incidence decreased then plateaued; incidence decreased further during early September and might be increasing. Percentage of positive test results decreased during August and plateaued during September. Underlying conditions were more common among school-aged children with severe outcomes related to COVID-19: among school-aged children who were hospitalized, admitted to an intensive care unit (ICU), or who died, 16%, 27%, and 28%, respectively, had at least one underlying medical condition. Schools and communities can implement multiple, concurrent mitigation strategies and tailor communications to promote mitigation strategies to prevent COVID-19 spread. These results can provide a baseline for monitoring trends and evaluating mitigation strategies.

41. **National Trends of Cases of COVID-19 in Children Based on US State Health Department Data.** Sisk B, Cull W, Harris JM, et al. *Pediatrics.* 2020. doi: 10.1542/peds.2020-027425
https://pediatrics.aappublications.org/content/pediatrics/early/2020/09/23/peds.2020-027425.full.pdf
Findings: As of Sept. 10, there were 549,432 cumulative child COVID-19 US cases, a rate of 729 cases per 100,000 children. There has been substantial variation in case growth by region: in April, a preponderance of cases was in the Northeast. In June, cases surged in the South and West, followed by mid-July increases in the Midwest. Over time, the proportion of COVID-19 cases that are pediatric has risen substantially, although below children's share of the US population (22.6%). While currently children represent 10% of the cumulative number of reported cases, the history behind that cumulative number shows substantial change. In April, less than 3% of the reported cases were pediatric. In the last 8 weeks, children represented between 12-15.9% of new weekly reported cases. Although children are a growing percentage of total cases, hospitalization, and death due to COVID-19 is uncommon. On Sept. 10, children represented 1.7% of total hospitalizations and about 2% of child cases resulted in

hospitalization. Children made up 0.07% of total deaths and 0.01% of child cases resulted in death.

42. **Multisystem Inflammatory Syndrome in Children Associated with Coronavirus Disease 2019 in a Children's Hospital in New York City: Patient Characteristics and an Institutional Protocol for Evaluation, Management, and Follow-Up.** Jonat B, Gorelik M, Boneparth A, et al. *Pediatr Crit Care Med*. 2020 Sep 29. doi: 10.1097/PCC.0000000000002598.
https://journals.lww.com/pccmjournal/Abstract/9000/Multisystem_Inflammatory_Syndrome_in_Children.97935.aspx
This report provides guidance to clinicians on evaluation, management, and follow-up of patients with a novel hyperinflammatory syndrome related to coronavirus disease 2019 known as multisystem inflammatory syndrome in children. It is based on the relevant literature and our experience. Instituting such a protocol during a global pandemic is feasible and is associated with patients receiving treatment and returning home more quickly.

GUIDELINES & CONSENSUS STATEMENTS

Caring for Critically Ill Children With Suspected or Proven Coronavirus Disease 2019 Infection: Recommendations by the Scientific Sections' Collaborative of the European Society of Pediatric and Neonatal Intensive Care. European Society of Pediatric and Neonatal Intensive Care (ESPNIC) Scientific Sections' Collaborative Group. *Pediatr Crit Care Med.* 2020 Sep 29. doi: 10.1097/PCC.0000000000002599.

Recommendations for antibacterial therapy in adults with COVID-19 - An evidence based guideline. Sieswerda E, De Boer MGJ, Bonten MMJ, et al. *Clin Microbiol Infect.* 2020 Sep 30:S1198-743X(20)30594-2. doi: 10.1016/j.cmi.2020.09.041.

FDA / CDC / NIH / WHO Updates

CDC - How COVID-19 Spreads, updated October 5, 2020 to include Airborne Transmission.

Commentary & Press Releases

Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 28 September - 1 October 2020

If you would like to receive a **customized COVID-19 Topic Alert** related to your specialty or area of interest, would like a **literature search** conducted, or have difficulty **accessing** any of the above articles please contact us at **librarian@providence.org**

Find previous weeks **here.**