Providence

COVID-19 Resource Desk

#18 | 8.19.2020 to 8.25.2020

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

Basic Science / Virology / Pre-clinical

1. **Immuno-epidemiology and pathophysiology of coronavirus disease 2019 (COVID-19).** Olwenyi OA, Dyavar SR, Acharya A, et al. *J Mol Med (Berl)*. 2020 Aug 18:1-15. doi: 10.1007/s00109-020-01961-4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7431311/
   Findings: We reviewed how changes in the SARS-CoV-2 genome and its structural architecture affect viral replication, immune evasion, and transmission within different human populations. We also looked at which immune dominant regions of SARS-CoV-2 and other coronaviruses are recognized by Major Histocompatibility Complex (MHC)/Human Leukocyte Antigens (HLA) genes and how this could impact on subsequent disease pathogenesis. Efforts were also placed on understanding immunological changes that occur when exposed individuals either remain asymptomatic or fail to control the virus and later develop systemic complications. Published autopsy studies that reveal alterations in the lung immune microenvironment, morphological, and pathological changes are also explored within the context of the review. Understanding the true correlates of protection and determining how constant virus evolution impacts on host-pathogen interactions could help identify which populations are at high risk and later inform future vaccine and therapeutic interventions.

2. **Artificial Intelligence for Rapid Meta-Analysis: Case Study on Ocular Toxicity of Hydroxychloroquine.** Matthew Michelson, Tiffany Chow, Neil A Martin, et al. [***PSJH authors***] *J Med Internet Res.* 2020 Aug 17;22(8):e20007. doi: 10.2196/20007. http://www.scielo.org.ar/pdf/aol/v30n2/v30n2a07.pdf
   Findings: By combining AI with human analysis in our RMA, we generated a meaningful, clinical result in less than 30 minutes. The RMA identified 11 studies considering ocular toxicity as a side effect of hydroxychloroquine and estimated the incidence to be 3.4% (95% CI 1.11%-9.96%). The heterogeneity across individual study findings was high, which should be taken into account in interpretation of the result. We demonstrate that a novel approach to meta-analysis using AI can generate meaningful clinical insights in a much shorter time period than traditional meta-analysis.

Clinical Syndrome

3. **COVID-19-Associated Coagulopathy: An Exacerbated Immunothrombosis Response.** Jayarangaiah A, Kariyanna PT, Chen X, Jayarangaiah A, Kumar A. *Clin Appl Thromb Hemost*. 2020 Jan-Dec;26:1076029620943293. doi: 10.1177/1076029620943293. https://journals.sagepub.com/doi/full/10.1177/1076029620943293
   Findings: COVID-associated coagulopathy (CAC) was recognized based on profound d-dimer elevations and evidence of microthrombi and macrothrombi, both in venous and arterial systems. The underlying mechanisms associated with CAC have been suggested, but not clearly defined. The model of immunothrombosis illustrates the elaborate crosstalk between the innate immune system and coagulation. The rendering of a procoagulant state in COVID-19 involves the interplay of many innate immune pathways. The SARS-CoV2 virus can directly infect immune and endothelial cells, leading to endothelial injury and dysregulation of the immune system. Activated leukocytes potentiate a procoagulant state via release of intravascular tissue factor, platelet activation, NETosis, and inhibition of anticoagulant mechanisms. Additional pathways of specific relevance in CAC include cytokine release and complement activation. All these mechanisms have recently been reported in COVID-19. Immunothrombosis provides a comprehensive perspective of the several synergistic pathways pertinent to the pathogenesis of CAC.
   > *See also*: **Pathogenesis and Treatment Strategies of COVID-19-Related Hypercoagulant and Thrombotic Complications.** Haimei MA. *Clin Appl Thromb Hemost.* 2020 Jan-Dec;26:1076029620944497. doi: 10.1177/1076029620944497.

4. **Cytotoxic lesions of the corpus callosum (CLOCCs) associated with SARS-CoV-2 infection.** Moreau A, Ego A, Vandergheynst F, et al. *J Neurol.* 2020 Aug 18:1-3. doi: 10.1007/s00415-020-10164-3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7433277/
   Findings: Here, we report a case of neurological symptoms associated with cytotoxic lesions of the corpus callosum (CLOCCs) in a COVID-19 patient.
   > *See also*: **Cytotoxic lesion of the corpus callosum as presenting neuroradiological manifestation of COVID-2019 infection.** Forestier G, de Beaurepaire I, Bornet G, Boulouis G. *J Neurol*. 2020 Aug 18:1-3. doi: 10.1007/s00415-020-10166-1.

5. **Acutely altered mental status as the main clinical presentation of multiple strokes in critically ill patients with COVID-19.** Díaz-Pérez C, Ramos C, López-Cruz A, et al. *Neurol Sci.* 2020 Aug 17:1-4. doi: 10.1007/s10072-020-04679-w. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7431112/
   Findings: Acutely altered mental status might be the main manifestation of multiple brain infarctions in critically ill COVID-19 patients. It should be specially considered in those with suspected COVID-19-associated coagulopathy. Full-dose anticoagulation and clinical-radiological monitoring might reduce their neurological consequences.

6. **Early Brain Imaging Shows Increased Severity of Acute Ischemic Strokes with Large Vessel Occlusion in COVID-19 Patients.** Escalard S, Chalumeau V, Escalard C, et al. *Stroke*. 2020 Aug 19:STROKEAHA120031011. doi: 10.1161/STROKEAHA.120.031011. https://www.ahajournals.org/doi/10.1161/STROKEAHA.120.031011

Findings: Twelve COVID-19 patients with anterior circulation large vessel occlusion and early brain imaging were included during the study period and compared with 34 control patients with anterior circulation large vessel occlusion and early brain imaging in 2019. Patients in the COVID-19 group were younger (P=0.032) and had a history of diabetes mellitus more frequently (P=0.039). Patients did not significantly differ on initial National Institutes of Health Stroke Scale nor time from onset to imaging (P=0.18 and P=0.6, respectively). Patients with COVID-19 had more severe strokes than patients without COVID-19, with a significantly lower clot burden score (median: 6.5 versus 8, P=0.016), higher rate of multivessel occlusion (50% versus 8.8%, P=0.005), lower DWI-ASPECTS (Diffusion-Weighted Imaging-Alberta Stroke Program Early Computed Tomography Scores; median: 5 versus 8, P=0.006), and higher infarct core volume (median: 58 versus 6 mL, P=0.004). Successful recanalization rate was similar in both groups (P=0.767). In-hospital mortality was higher in the COVID-19 patients' group (41.7% versus 11.8%, P=0.025). Early brain imaging showed higher severity large vessel occlusion strokes in patients with COVID-19. Given the massive number of infected patients, concerns should be raised about the coming neurovascular impact of the pandemic worldwide.

7. **Effects of a major deletion in the SARS-CoV-2 genome on the severity of infection and the inflammatory response: an observational cohort study.** Young BE, Fong SW, Chan YH, et al. *Lancet*. August 18, 2020DOI:https://doi.org/10.1016/S0140-6736(20)31757-8 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31757-8/fulltext
Findings: The Δ382 variant of SARS-CoV-2 seems to be associated with a milder infection. The observed clinical effects of deletions in ORF8 could have implications for the development of treatments and vaccines.

8. **Characterization of Patients Who Return to Hospital Following Discharge from Hospitalization for COVID-19.** Somani SS, Richter F, Fuster V, et al. *J Gen Intern Med.* 2020 Aug 19:1-7. doi: 10.1007/s11606-020-06120-6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7274228/
Findings: Of 2864 discharged patients, 103 (3.6%) returned for emergency care after a median of 4.5 days, with 56 requiring inpatient readmission. The most common reason for return was respiratory distress (50%). Compared with patients who did not return, there were higher proportions of COPD (6.8% vs 2.9%) and hypertension (36% vs 22.1%) among those who returned. Patients who returned also had a shorter median length of stay (LOS) during index hospitalization (4.5 [2.9,9.1] vs 6.7 [3.5, 11.5] days; Padjusted = 0.006), and were less likely to have required intensive care on index hospitalization (5.8% vs 19%; Padjusted = 0.001). A trend towards association between absence of in-hospital treatment-dose anticoagulation on index admission and return to hospital was also observed (20.9% vs 30.9%, Padjusted = 0.06). On readmission, rates of intensive care and death were 5.8% and 3.6%, respectively. Return to hospital after admission for COVID-19 was infrequent within 14 days of discharge. The most common cause for return was respiratory distress. Patients who returned more likely had COPD and hypertension, shorter LOS on index-hospitalization, and lower rates of in-hospital treatment-dose anticoagulation. Future studies should focus on whether these comorbid conditions, longer LOS, and anticoagulation are associated with reduced readmissions.

Diagnostics & Screening

9. **Humoral Immune Response to SARS-CoV-2.** Herroelen PH, Martens GA, De Smet D, Swaerts K, Decavele AS. *Am J Clin Pathol.* 2020 Aug 18:aqaa140. doi: 10.1093/ajcp/aqaa140. https://academic.oup.com/ajcp/advance-article/doi/10.1093/ajcp/aqaa140/5893931
Findings: Wantai SARS-COV-2 Ab ELISA and Orient Gene COVID-19 IgG/IgM Rapid Test showed superior overall sensitivity for detection of SARS-CoV-2 antibodies. Elecsys Anti-SARS-CoV-2 assay and EUROIMMUN Anti-SARS-CoV-2 combined IgG/IgA showed acceptable sensitivity (>95%) vs the consensus result of all assays from 10 days post onset of symptoms. Wantai SARS-COV-2 Ab ELISA, Elecsys Anti-SARS-CoV-2 assay, and Innovita 2019-nCoV Ab rapid test showed least cross-reactivity, resulting in an optimal analytical specificity greater than 98%. Wantai SARS-COV-2 Ab ELISA and Elecsys Anti-SARS-CoV-2 assays are suitable for sensitive and specific detection of SARS-CoV-2 antibodies from 10 days after onset of symptoms.

10. **ORF8 and ORF3b antibodies are accurate serological markers of early and late SARS-CoV-2 infection.** Hachim A, Kavian N, Cohen CA, et al. *Nat Immunol.* 2020 Aug 17. doi: 10.1038/s41590-020-0773-7. https://www.nature.com/articles/s41590-020-0773-7
Findings: In this study, we utilized the luciferase immunoprecipitation system to assess the antibody responses to 15 different SARS-CoV-2 antigens in patients with COVID-19. We identified new targets of the immune response to SARS-CoV-2 and show that nucleocapsid, open reading frame (ORF)8 and ORF3b elicit the strongest specific antibody responses. ORF8 and ORF3b antibodies, taken together as a cluster of points, identified 96.5% of COVID-19 samples at early and late time points of disease with 99.5% specificity. Our findings could be used to develop second-generation diagnostic tests to improve serological assays for COVID-19 and are important in understanding pathogenicity.

11. **Nucleic Acid Testing for Coronavirus Disease 2019: Demand, Research Progression, and Perspective.** Zhang S, Su X, Wang J, et al. *Crit Rev Anal Chem*. 2020 Aug 19:1-12. doi: 10.1080/10408347.2020.1805294.
https://www.tandfonline.com/doi/full/10.1080/10408347.2020.1805294
Findings: There has been a surge in demand for COVID-19 diagnostic reagents, as timely detection of virus carriers is one of the most important components of disease prevention and control. Nucleic acid testing (NAT), with high sensitivity and specificity, is considered the "gold standard" for the diagnosis of COVID-19. Therefore, more than 700 research units and companies have been devoted to developing NAT reagents. To date, nearly 600 research units and companies have claimed to have completed the development of NAT reagents. The use of these products has a positive effect on disease prevention and control; however, exaggerated claims and inadequate understanding of the products have led to improper access to reagents and equipment in clinics. This has resulted in chaos in the clinical diagnosis of COVID-19. Herein, we have overviewed the COVID-19 NAT products, including their principles, corresponding advantages and disadvantages, relevant circumstances for application, and respective roles in epidemic containment. Our comments may provide some references for assay developers and aid clinical staff in choosing the appropriate class of test from the different tests available.

12. **Chest CT for rapid triage of patients in multiple emergency departments during COVID-19 epidemic: experience report from a large French university hospital.** Ducray V, Vlachomitrou AS, Bouscambert-Duchamp M, et al. *Eur Radiol.* 2020 Aug 19:1-9. doi: 10.1007/s00330-020-07154-4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7435221/
Findings: • In a large university hospital in Lyon, France, the accuracy, sensitivity, specificity, PPV, and NPV of chest CT for COVID-19 reached 88.9%, 90.2%, 88%, 84.1%, and 92.7%, respectively, using RT-PCR as standard of reference. • The mean delay for CT reports was three times shorter than for RT-PCR results (187 ± 148 min versus 573 ± 327 min, $p < 0.0001$). • Due to high accuracy of chest CT for COVID-19 and shorter time for CT reports than RT-PCR results, chest CT can be used to orient patients suspected to be positive towards the COVID+ unit to decrease congestion in the emergency departments.

13. **Interest of the cellular population data analysis as an aid in the early diagnosis of SARS-CoV-2 infection.** Vasse M, Ballester MC, Ayaka D, et al. *Int J Lab Hematol*. 2020 Aug 19. doi: 10.1111/ijlh.13312. https://onlinelibrary.wiley.com/doi/10.1111/ijlh.13312
Findings: Among 222 patients, 86 were diagnosed as COVID-19 and 60.5% were correctly identified using the discriminating protocol. Among the 136 COVID patients, 10.3% were misclassified (specificity 89.7%, sensitivity 60.5%). False negatives were observed mainly in patients with a low inflammatory state whereas false positives were mainly seen in patients with sepsis. Consideration of CPD could constitute a first step and potentially aid in the early diagnosis of COVID-19.

14. **A highly specific and sensitive serological assay detects SARS-CoV-2 antibody levels in COVID-19 patients that correlate with neutralization.** Peterhoff D, Glück V, Vogel M, et al. *Infection*. 2020 Aug 21. doi: 10.1007/s15010-020-01503-7.
https://link.springer.com/article/10.1007/s15010-020-01503-7
Findings: With the described RBD-based ELISA protocol, we provide a reliable test for seroepidemiological surveys. Due to high specificity and strong correlation with virus neutralization, the RBD ELISA holds great potential to become a preferred tool to assess thresholds of protective immunity after infection and vaccination.

Epidemiology & Public Health

15. **COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing.** To KK, Hung IF, Ip JD, et al. *Clinical Infectious Diseases*, ciaa1275, https://doi.org/10.1093/cid/ciaa1275
https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1275/5897019
Findings: Whole genome sequencing was performed directly on respiratory specimens collected during two episodes of COVID-19 in a patient. Comparative genome analysis was conducted to differentiate re-infection from persistent viral shedding. The second episode of asymptomatic infection occurred 142 days after the first symptomatic episode in an apparently immunocompetent patient. During the second episode, there was serological evidence of elevated C-reactive protein and SARS-CoV-2 IgG seroconversion. Viral genomes from first and second episodes belong to different clades/lineages. Compared to viral genomes in GISAID, the

first virus genome has a stop codon at position 64 of orf8 leading to a truncation of 58 amino acids, and was phylogenetically closely related to strains collected in March/April 2020, while the second virus genome was closely related to strains collected in July/August 2020. Another 23 nucleotide and 13 amino acid differences located in 9 different proteins, including positions of B and T cell epitopes, were found between viruses from the first and second episodes. Epidemiological, clinical, serological and genomic analyses confirmed that the patient had re-infection instead of persistent viral shedding from first infection. Our results suggest SARS-CoV-2 may continue to circulate among the human populations despite herd immunity due to natural infection or vaccination.

16. **Years of Life Lost Attributable to COVID-19 in High-incidence Countries.** Oh IH, Ock M, Jang SY, et al. *J Korean Med Sci.* 2020 Aug 17;35(32):e300. doi: 10.3346/jkms.2020.35.e300. https://jkms.org/search.php?where=aview&id=10.3346/jkms.2020.35.e300&code=0063JKMS&vmode=PUBREADER
Findings: As of April 22, 2020, there were 1,699,574 YLLs due to COVID-19 in 30 high-incidence countries. On July 14, 2020, this increased to 4,072,325. Both on April 22 and July 14, the total YLLs due to COVID-19 was highest in the USA (April 22, 534,481 YLLs; July 14, 1,199,510 YLLs), and the YLLs per 100,000 population was highest in Belgium (April 22, 868.12 YLLs/100,000; July 14, 1,593.72 YLLs/100,000). YLLs due to COVID-19 were higher among males than among females and higher in those aged ≥ 60 years than in younger individuals. Belgium had the highest proportion of YLLs attributable to COVID-19 as a proportion of the total YLLs and the highest disability-adjusted life years per 100,000 population. This study estimated YLLs due to COVID-19 in 30 countries. COVID-19 is a high burden in the USA and Belgium, among males and the elderly. The YLLs are very closely related with the incidence as well as the mortality. This highlights the importance of the early detection of incident case that minimizes severe acute respiratory syndrome coronavirus-2 fatality.

17. **The epidemiological burden of and overall distribution of chronic comorbidities in coronavirus disease-2019 among 202,005 infected patients: evidence from a systematic review and meta-analysis.** Mahumud RA, Kamara JK, Renzaho AMN. *Infection*. 2020 Aug 19:1-21. doi: 10.1007/s15010-020-01502-8. https://link.springer.com/article/10.1007/s15010-020-01502-8
Findings: A median age of COVID-19 patients was 56.4 years and 55% of the patients were male. The most prevalent chronic comorbid conditions: any type of chronic comorbidity (37%), hypertension (22%), diabetes (14%), respiratory diseases (5%), cardiovascular diseases (13%) and other chronic diseases (e.g., cancer) (8%). Furthermore, 37% of COVID-19 patients had at least one chronic comorbid condition, 28% of patients had two conditions, and 19% of patients had three or more chronic conditions. The overall pooled CFR was 7% (95% CI 6-7%). The crude CFRs increased significantly with increasing number of chronic comorbid conditions, ranging from 6% for at least one chronic comorbid condition to 13% for 2 or 3 chronic comorbid conditions, 12% for 4 chronic comorbid conditions, 14% for 5 chronic comorbid conditions, and 21% for 6 or more chronic comorbid conditions. Furthermore, the overall CFRs also significantly increased with higher levels of reported clinical symptoms, ranging from 14% for at least four symptoms, to 15% for 5 or 6 symptoms, and 21% for 7 or more symptoms. The chronic

comorbid conditions were identified as dominating risk factors, which should be considered in an emergency disease management and treatment choices. There is urgent need to further enhance systematic and real-time sharing of epidemiologic data, clinical results, and experience to inform the global response to COVID-19.

18. **Health Policy Perspective: Medicaid and State Politics beyond COVID.** Zhu JM, Grande D, Jones DK, Tipirneni R. *J Gen Intern Med*. 2020 Aug 19:1-3. doi: 10.1007/s11606-020-06117-1. https://link.springer.com/article/10.1007/s11606-020-06117-1
Findings: The COVID-19 pandemic is poised to drastically alter the Medicaid program. While state Medicaid programs are currently expanding coverage policies and enrollment to address acute public health needs, states will soon face significant budget shortfalls. These impending changes may renew partisan debates about restrictive policies like work requirements, which generally require beneficiaries to verify their participation in certain activities-such as employment, job search, or training programs-in order to receive or retain coverage. We argue that restrictive Medicaid policies are driven, to a great extent, by political party affiliation, highlighting the outsized role of partisanship in Medicaid policy adoption. To combat these dynamics, additional efforts are needed to improve community-informed decision-making, strengthen evaluation approaches to tie evidence to policymaking, and boost participation in and understanding of the political processes that affect policy change.

19. **Differences in US COVID-19 case rates and case fatality rates across the urban-rural continuum.** Pro G, Hubach R, Wheeler D, et al. *Rural Remote Health*. 2020 Aug;20(3):6074. doi: 10.22605/RRH6074. Epub 2020 Aug 19. https://www.rrh.org.au/journal/article/6074
Findings: COVID-19 public health and media messaging in the USA has focused on major outbreaks in densely populated urban areas, including New York City, New Orleans and Seattle. The mortality burden of COVID-19 is exceptionally high in rural areas in the USA, despite the country's overall lower rate of cases. These findings highlight the need to concentrate resources in not only areas where case rates and crude numbers of deaths are high, but also underserved rural areas where the case fatality rate is disproportionately high. Many rural areas face substantial challenges in disease surveillance, testing and treatment. Challenges range from hospital capacity, long distances between residences and testing sites, access to life-saving treatment such as ventilators, and underlying health and socioeconomic conditions that may exacerbate the severity of COVID-19 infections.

20. **How Do Presenting Symptoms and Outcomes Differ by Race/Ethnicity Among Hospitalized Patients with COVID-19 Infection? Experience in Massachusetts.** McCarty TR, Hathorn KE, Redd WD, et al. *Clin Infect Dis*. 2020 Aug 22:ciaa1245. doi: 10.1093/cid/ciaa1245. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1245/5896009
Findings: Latinx patients were younger, had fewer cardiopulmonary disorders, were more likely to have obesity, more frequently reported fever and myalgia, and had lower D-dimer levels compared to White patients. On multivariable analysis controlling for age, gender, obesity, cardiopulmonary comorbidities, hypertension, and diabetes, no significant differences in in-hospital mortality, ICU admission, or mechanical ventilation by race/ethnicity were found. Diabetes was a significant predictor for mechanical ventilation while older age was a predictor

of in-hospital mortality. In this multi-center cohort of hospitalized COVID-19 patients in the largest health system in Massachusetts, there was no association between race/ethnicity and clinically relevant hospitalization outcomes, including in-hospital mortality, after controlling for key demographic/clinical characteristics. These findings serve to refute suggestions that certain races/ethnicities may be biologically predisposed to poorer COVID-19 outcomes.

21. **Estimating unobserved SARS-CoV-2 infections in the United States.** Perkins TA, Cavany SM, Moore SM, et al. *Proc Natl Acad Sci U S A*. 2020 Aug 21:202005476. doi: 10.1073/pnas.2005476117. https://www.pnas.org/content/early/2020/08/20/2005476117
Findings: We developed an approach for estimating the number of unobserved infections based on data that are commonly available shortly after the emergence of a new infectious disease. The logic of our approach is, in essence, that there are bounds on the amount of exponential growth of new infections that can occur during the first few weeks after imported cases start appearing. Applying that logic to data on imported cases and local deaths in the United States through 12 March, we estimated that 108,689 (95% posterior predictive interval [95% PPI]: 1,023 to 14,182,310) infections occurred in the United States by this date. By comparing the model's predictions of symptomatic infections with local cases reported over time, we obtained daily estimates of the proportion of symptomatic infections detected by surveillance. This revealed that detection of symptomatic infections decreased throughout February as exponential growth of infections outpaced increases in testing. Between 24 February and 12 March, we estimated an increase in detection of symptomatic infections, which was strongly correlated (median: 0.98; 95% PPI: 0.66 to 0.98) with increases in testing. These results suggest that testing was a major limiting factor in assessing the extent of SARS-CoV-2 transmission during its initial invasion of the United States.

22. **Risk for Severe COVID-19 Illness Among Teachers and Adults Living with School-Aged Children.** Gaffney AW, Himmelstein D, Woolhandler S. *Ann Intern Med*. 2020 Aug 21. doi: 10.7326/M20-5413. https://www.acpjournals.org/doi/10.7326/M20-5413
Findings: We analyzed nationally representative data from the 2018 National Health Interview Survey. We used the Centers for Disease Control and Prevention's criteria (3) to define “definite” and “possible” risk factors for severe COVID-19 illness, including differing severities of obesity, and tabulated their prevalence among 3 groups: employed adults other than teachers, adults employed as teachers, and adults living with school-aged (aged 5 to 17 years) children. About 40 million U.S. adults who work or live with school-aged children have definite or possible risk factors for severe COVID-19 illness, a number that excludes 4.4 million nonteachers working at schools and 1.6 million day care workers (Himmelstein DU. Unpublished data). Adults living with Black children and those living with children in low-income households are at especially high risk; teachers' risk seems similar to that of other working adults.

23. **SARS-CoV-2 Community Transmission disproportionately affects Latinx population during Shelter-in-Place in San Francisco.** Chamie G, Marquez C, Crawford E, et al. *Clin Infect Dis*. 2020 Aug 21:ciaa1234. doi: 10.1093/cid/ciaa1234. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1234/5895337

Findings: We tested 3,953 persons: 40% Latinx; 41% White; 9% Asian/Pacific Islander; and 2% Black. Overall, 2.1% (83/3,871) tested PCR-positive: 95% were Latinx and 52% asymptomatic when tested. 1.7% of census tract residents and 6.0% of workers (non-census tract residents) were PCR-positive. Among 2,598 tract residents, estimated point prevalence of PCR-positives was 2.3% (95%CI: 1.2-3.8%): 3.9% (95%CI: 2.0-6.4%) among Latinx vs. 0.2% (95%CI: 0.0-0.4%) among non-Latinx persons. Estimated cumulative incidence among residents was 6.1% (95%CI: 4.0-8.6%). Prior infections were 67% Latinx, 16% White, and 17% other ethnicities. Among recent infections, 96% were Latinx. Risk factors for recent infection were Latinx ethnicity, inability to shelter-in-place and maintain income, frontline service work, unemployment, and household income &$50,000/year. Five SARS-CoV-2 phylogenetic lineages were detected. SARS-CoV-2 infections from diverse lineages continued circulating among low-income, Latinx persons unable to work from home and maintain income during San Francisco's shelter-in-place ordinance.

24. **Trends in Number and Distribution of COVID-19 Hotspot Counties - United States, March 8-July 15, 2020.** Oster AM, Kang GJ, Cha AE, et al. *MMWR Morb Mortal Wkly Rep*. 2020 Aug 21;69(33):1127-1132. doi: 10.15585/mmwr.mm6933e2. https://www.cdc.gov/mmwr/volumes/69/wr/mm6933e2.htm
Findings: During March 8-July 15, 2020, 818 counties met hotspot criteria for ≥1 day; these counties included 80% of the U.S. population. The daily number of counties meeting hotspot criteria peaked in early April, decreased and stabilized during mid-April-early June, then increased again during late June-early July. The percentage of counties in the South and West Census regions meeting hotspot criteria increased from 10% and 13%, respectively, during March-April to 28% and 22%, respectively, during June-July. Identification of community transmission as a contributing factor increased over time, whereas identification of outbreaks in long-term care facilities, food processing facilities, correctional facilities, or other workplaces as contributing factors decreased. Identification of hotspot counties and understanding how they change over time can help prioritize and target implementation of U.S. public health response activities.

25. **Determinants of COVID-19 vaccine acceptance in the US.** Malik AA, McFadden SM, Elharake J, Omer SB. *EClinicalMedicine.* 2020 Aug 12:100495. doi: 10.1016/j.eclinm.2020.100495. https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30239-X/fulltext
FINDINGS: Of the 672 participants surveyed, 450 (67%) said they would accept a COVID-19 vaccine if it is recommended for them. Males (72%) compared to females, older adults (≥55 years; 78%) compared to younger adults, Asians (81%) compared to other racial and ethnic groups, and college and/or graduate degree holders (75%) compared to people with less than a college degree were more likely to accept the vaccine. When comparing reported influenza vaccine uptake to reported acceptance of the COVID-19 vaccine: 1) participants who did not complete high school had a very low influenza vaccine uptake (10%), while 60% of the same group said they would accept the COVID-19 vaccine; 2) unemployed participants reported lower influenza uptake and lower COVID-19 vaccine acceptance when compared to those employed or retired; and, 3) Black Americans reported lower influenza vaccine uptake and lower COVID-19 vaccine acceptance than all other racial groups reported in our study. Lastly,

we identified geographic differences with Department of Health and Human Services (DHHS) regions 2 (New York) and 5 (Chicago) reporting less than 50 percent COVID-19 vaccine acceptance. Although our study found a 67% acceptance of a COVID-19 vaccine, there were noticeable demographic and geographical disparities in vaccine acceptance. Before a COVID-19 vaccine is introduced to the U.S., public health officials and policymakers must prioritize effective COVID-19 vaccine-acceptance messaging for all Americans, especially those who are most vulnerable.

Healthcare Delivery & Healthcare Workers

26. **The National COVID Cohort Collaborative (N3C): Rationale, Design, Infrastructure, and Deployment.** Melissa H, Christopher C, Kenneth G. *J Am Med Inform Assoc*. 2020 Aug 17:ocaa196. doi: 10.1093/jamia/ocaa196. https://academic.oup.com/jamia/advance-article/doi/10.1093/jamia/ocaa196/5893482
Findings: COVID-19 poses societal challenges that require expeditious data and knowledge sharing. Though medical records are abundant, they are largely inaccessible to outside researchers. Statistical, machine learning, and causal research are most successful with large datasets beyond what is available in any given organization. Here, we introduce the National COVID Cohort Collaborative (N3C), an open science community focused on analyzing patient-level data from many clinical centers to reveal patterns in COVID-19 patients. To create N3C, the community had to overcome technical, regulatory, policy, and governance barriers to sharing patient-level clinical data. In less than 2 months, we developed solutions to acquire and harmonize data across organizations and created a secure data environment to enable transparent and reproducible collaborative research. We expect the N3C to help save lives by enabling collaboration among clinicians, researchers, and data scientists to identify treatments and specialized care needs and thereby reduce the immediate and long-term impacts of COVID-19.

27. **Telecritical Care Clinical and Operational Strategies in Response to COVID-19.** Singh J, Green MB, Lindblom S, et al. *Telemed J E Health*. 2020 Aug 17. doi: 10.1089/tmj.2020.0186. https://www.liebertpub.com/doi/full/10.1089/tmj.2020.0186
Findings: We propose strategic initiatives by which TCC may act as a force multiplier for pandemic preparedness in response to COVID-19, utilizing a tiered approach for increasing surge capacity needs. The goals involved usage of TCC to augment ICU capacity, optimize safety, minimize personal protective equipment (PPE) use, improve efficiencies, and enhance knowledge of managing pandemic response. Implementation Phase: A phased approach utilizing TCC would involve implementing remote capabilities across the enterprise to accomplish the goals outlined. The hardware and software needed for initial expansion to cover 275 beds included $956,670 for mobile carts and $173,106 for home workstations. Team role deployment and bedside clinical care centering around TCC as critical care capacity expand beyond 275 beds. Surge capacity was not reached during early phases of the pandemic in the region, allowing refinement of TCC during subsequent pandemic phases. Conclusions: Leveraging TCC facilitated pandemic surge planning but required redefinition of typical ICU staffing models. The design was meant to workforce efficiencies, reduce PPE use, and minimize

health care worker exposure risk, all while maintaining quality care standards through an intensivist-led model. As health care operations resumed and states reopened, TCC is being used to support shifts in volume and critical care personnel during the pandemic evolution. The lessons applied may help health care systems through variable phases of the pandemic.

28. **Usefulness and safety of a dedicated team to prone patients with severe ARDS due to COVID-19.** Kimmoun A, Levy B, Chenuel B; DV-Team group. *Crit Care.* 2020 Aug 18;24(1):509. doi: 10.1186/s13054-020-03128-6. https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-03128-6
Findings: Facing the coronavirus disease 2019 (COVID-19) pandemic, prone positioning (PP) is of crucial importance to treat severe ARDS patients [2]. Nevertheless, the high number of ICU admissions quickly overwhelmed the ability of the daily ICU team to place patients in PP, a complex and time-consuming maneuver. Thus, we created a dedicated medical team with reassigned volunteers to cope with the large number of patients requiring PP.

29. **Addressing Postpandemic Clinician Mental Health: A Narrative Review and Conceptual Framework.** Schwartz R, Sinskey JL, Anand U, Margolis RD. *Ann Intern Med.* 2020 Aug 21. doi: 10.7326/M20-4199. https://www.acpjournals.org/doi/10.7326/M20-4199
Findings: Previous pandemics have seen high psychiatric morbidity among health care workers. Protecting clinician mental health in the aftermath of coronavirus disease 2019 (COVID-19) requires an evidence-based approach to developing and deploying comprehensive clinician mental health support. In a narrative review of 96 articles addressing clinician mental health in COVID-19 and prior pandemics, 7 themes emerged: 1) the need for resilience and stress reduction training; 2) providing for clinicians' basic needs (food, drink, adequate rest, quarantine-appropriate housing, transportation, child care, personal protective equipment); 3) the importance of specialized training for pandemic-induced changes in job roles; 4) recognition and clear communication from leadership; 5) acknowledgment of and strategies for addressing moral injury; 6) the need for peer and social support interventions; and 7) normalization and provision of mental health support programs. In addition to the literature review, in collaboration with the Collaborative for Healing and Renewal in Medicine (CHARM) network, the authors gathered practice guidelines and resources from health care organizations and professional societies worldwide to synthesize a list of resources deemed high-yield by well-being leaders. Studies of previous pandemics demonstrate heightened distress in health care workers years after the event. The COVID-19 pandemic presents unique challenges that surpass those of previous pandemics, suggesting a significant mental health toll on clinicians. Long-term, proactive individual, organizational, and societal infrastructures for clinician mental health support are needed to mitigate the psychological costs of providing care during the COVID-19 pandemic.

30. **Differential occupational risks to healthcare workers from SARS-CoV-2 observed during a prospective observational study.** Eyre DW, Lumley SF, O'Donnell D, et al. *Elife*. 2020 Aug 21;9:e60675. doi: 10.7554/eLife.60675. https://elifesciences.org/articles/60675
Findings: We conducted voluntary Covid-19 testing programmes for symptomatic and asymptomatic staff at a UK teaching hospital using naso-/oro-pharyngeal PCR testing and

immunoassays for IgG antibodies. 1128/10,034(11.2%) staff had evidence of Covid-19 at some time. Using questionnaire data provided on potential risk-factors, staff with a confirmed household contact were at greatest risk. Higher rates of Covid-19 were seen in staff working in Covid-19-facing areas (22.6% vs. 8.6% elsewhere). Controlling for Covid-19-facing status, risks were heterogenous across the hospital, with higher rates in acute medicine and sporadic outbreaks in areas with few or no Covid-19 patients. Covid-19 intensive care unit staff were relatively protected, likely by a bundle of PPE-related measures. Positive results were more likely in Black and Asian staff, independent of role or working location, and in porters and cleaners.

31. **Chronic hospital nurse understaffing meets COVID-19: an observational study.** Lasater KB, Aiken LH, Sloane DM, et al. *BMJ Qual Saf*. 2020 Aug 18:bmjqs-2020-011512. doi: 10.1136/bmjqs-2020-011512.
https://qualitysafety.bmj.com/content/early/2020/08/13/bmjqs-2020-011512
Findings: Mean staffing in medical-surgical units varied from 3.3 to 9.7 patients per nurse, with the worst mean staffing in New York City. Over half the nurses in both states experienced high burnout. Half gave their hospitals unfavourable safety grades and two-thirds would not definitely recommend their hospitals. One-third of patients rated their hospitals less than excellent and would not definitely recommend it to others. After adjusting for confounding factors, each additional patient per nurse increased odds of nurses and per cent of patients giving unfavourable reports; ORs ranged from 1.15 to 1.52 for nurses on medical-surgical units and from 1.32 to 3.63 for nurses on intensive care units. Hospital nurses were burned out and working in understaffed conditions in the weeks prior to the first wave of COVID-19 cases, posing risks to the public's health. Such risks could be addressed by safe nurse staffing policies currently under consideration.

Laboratory Results

32. **Evaluating the Association of Clinical Characteristics with Neutralizing Antibody Levels in Patients Who Have Recovered from Mild COVID-19 in Shanghai, China.** Wu F, Liu M, Wang A, et al. *JAMA Intern Med.* 2020 Aug 18. doi: 10.1001/jamainternmed.2020.4616.
https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2769741
Findings: In this cohort study, among 175 patients who recovered from mild COVID-19 in Shanghai, China, NAb titers to SARS-CoV-2 appeared to vary substantially. Further research is needed to understand the clinical implications of differing NAb titers for protection against future infection.

33. **Changes in serum virus-specific IgM/IgG antibody in asymptomatic and discharged patients with reoccurring positive COVID-19 nucleic acid test (RPNAT).** Liu J, Lian R, Zhang G, et al. *Ann Med.* 2020 Aug 18:1-14. doi: 10.1080/07853890.2020.1811887.
https://www.tandfonline.com/doi/full/10.1080/07853890.2020.1811887
Findings: The best overall performance was found by combining the IgM, IgG, and CT; 95.1% sensitivity and 75% specificity. This was tested in 111 RT-PCR positive cases. The median IgM and IgG levels were lower in the asymptomatic group compared to the symptomatic group (P <

0.01). Among 15 RPNAT cases, the IgM levels of the RPNAT group at the time of discharge (IgM2.79, IQR: 0.95-5.37) and retest (IgM 2.35, IQR: 0.88-8.65) were significantly higher than those of the non-reoccurring positive nucleic acid test group (Non-RPNAT) (IgM on discharge: 0.59, IQR: 0.33-1.22, IgG on retest: 0.92, IQR: 0.51-1.58).Conclusion Serum SARS-CoV-2 specific IgM/IgG antibody levels remained at a low level during hospitalization for asymptomatic patients. Elevated IgM levels may have implications in the identification of RPNAT patients before discharge.

Prognosis

34. **COVID-19-Associated Critical Illness-Report of the First 300 Patients Admitted to Intensive Care Units at a New York City Medical Center.** Chand S, Kapoor S, Orsi D, et al. *J Intensive Care Med.* 2020 Oct;35(10):963-970. doi: 10.1177/0885066620946692. https://journals.sagepub.com/doi/full/10.1177/0885066620946692
Findings: Our first 300 ICU patients were admitted March 10 through April 11, 2020. The majority (60.7%) of patients were men. ARDS was documented in 91.7% of patients; 91.3% required mechanical ventilation. Prone positioning was employed in 58% of patients and neuromuscular blockade in 47.8% of mechanically-ventilated patients. Neither intervention was associated with decreased mortality. Vasopressors were required in 77.7% of patients. Acute kidney injury (AKI) was present on admission in 40.7% of patients, and developed subsequently in 36.0%; 50.9% of patients with AKI received renal replacement therapy (RRT). Overall 30-day mortality rate was 52.3%, and 55.8% among patients receiving mechanical ventilation. In univariate analysis, higher mortality rate was associated with increasing age, male sex, hypertension, obesity, smoking, number of comorbidities, AKI on presentation, and need for vasopressor support. A representative multivariable model for 30-day mortality is also presented, containing patient age, gender, body mass index, and AKI at admission. As of May 11, 2020, 2 patients (0.7%) remained hospitalized. Mortality in critical illness associated with COVID-19 is high. The majority of patients develop ARDS requiring mechanical ventilation, vasopressor-dependent shock, and AKI. The variation in mortality rates reported to date likely reflects differences in the severity of illness of the evaluated populations.

35. **Clinical characteristics and prognosis of hospitalized COVID-19 patients with incident sustained tachyarrhythmias: a multicenter observational study.** Russo V, Di Maio M, Mottola F, et al. *Eur J Clin Invest*. 2020 Aug 19:e13387. doi: 10.1111/eci.13387. https://onlinelibrary.wiley.com/doi/abs/10.1111/eci.13387
Findings: 414 hospitalized patients with COVID-19 (66.9 ± 15.0 years, 61.1% male) were included in the present study. During a median follow-up of 28 days (IQR: 12- 45), the most frequent incident sustained arrhythmia was AF, of which 12.1% were new-onset and 5.1% were recurrent, followed by VT and supraventricular arrhythmias. Incident AF, both new-onset and recurrent, did not affect the risk of severe adverse events including ARDS and death during hospitalization; in contrast incident VT significantly increased the risk of in-hospital mortality. AF is the more frequent incident tachyarrhythmia; however, it doesn't seem associated to ARDS development and death. On the other hand, incident VT is a not frequent but independent predictor of in-hospital mortality among hospitalized COVID-19 patients.

36. **Newly-diagnosed diabetes and admission hyperglycemia predict COVID-19 severity by aggravating respiratory deterioration.** Paolo Fadini G, Luca Morieri M, Boscari F, et al. *Diabetes Res Clin Pract.* 2020 Aug 14:108374. doi: 10.1016/j.diabres.2020.108374. https://www.diabetesresearchclinicalpractice.com/article/S0168-8227(20)30627-6/fulltext
Findings: 413 subjects were included, 107 of whom (25.6%) had diabetes, including 21 newly-diagnosed. Higher glucose level at admission was associated with COVID-19 severity, with a stronger association among patients without as compared to those with pre-existing diabetes. Admission glucose was correlated with most clinical severity indexes and its association with adverse outcome was mostly mediated by a worse respiratory function. Newly-diagnosed diabetes and admission hyperglycemia are powerful predictors of COVID-19 severity due to rapid respiratory deterioration.

37. **A dynamic COVID-19 immune signature includes associations with poor prognosis.** Laing AG et al. *Nat Med.* 2020 Aug 17. doi: 10.1038/s41591-020-1038-6. https://www.nature.com/articles/s41591-020-1038-6
Findings: We have identified a core peripheral blood immune signature across 63 hospital-treated patients with COVID-19 who were otherwise highly heterogeneous. The signature includes discrete changes in B and myelomonocytic cell composition, profoundly altered T cell phenotypes, selective cytokine/chemokine upregulation and SARS-CoV-2-specific antibodies. Some signature traits identify links with other settings of immunoprotection and immunopathology; others, including basophil and plasmacytoid dendritic cell depletion, correlate strongly with disease severity; while a third set of traits, including a triad of IP-10, interleukin-10 and interleukin-6, anticipate subsequent clinical progression. Hence, contingent upon independent validation in other COVID-19 cohorts, individual traits within this signature may collectively and individually guide treatment options; offer insights into COVID-19 pathogenesis; and aid early, risk-based patient stratification that is particularly beneficial in phasic diseases such as COVID-19.

38. **Anaemia is associated with severe illness in COVID-19: a retrospective cohort study.** Tao Z, Xu J, Chen W, et al. *J Med Virol*. 2020 Aug 19. doi: 10.1002/jmv.26444. https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.26444
Findings: In our cohort, compared to patients without anaemia, patients with anaemia were more likely to have one or more comorbidities and severe COVID-19 illness. More patients demonstrated elevated levels of C-reactive protein (CRP), procalcitonin (PCT) and creatinine in anaemia group. Levels of erythrocyte sedimentation rate (ESR), D-dimer, myoglobin, T-pro brain natriuretic peptide (T-pro-BNP) and urea nitrogen (BUN) in patients with anaemia were significantly higher than those without. Anaemia is an independent risk factor associated with the severe illness of COVID-19, and healthcare professionals should be more sensitive to the haemoglobin levels of COVID-19 patients on admission. Awareness of anemia as a risk factor for COVID-19 was of great significance.

39. **Circulating Endothelial Cells as a Marker of Endothelial Injury in Severe COVID-19.** Guervilly C, Burtey S, Sabatier F, et al. *J Infect Dis*. 2020 Aug 19:jiaa528. doi: 10.1093/infdis/jiaa528. https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa528/5894144
Findings: The objective of this study was to investigate whether increased levels of circulating endothelial cells (CEC) might be associated with severe forms of COVID-19. Ninety-nine patients with COVID-19 were enrolled in this retrospective study. Patients in the intensive care units (ICU) had significantly higher CEC counts than non-ICU patients and the extent of endothelial injury was correlated with putative markers of disease severity and inflammatory cytokines. Altogether, these data provide in vivo evidence that endothelial injury is a key feature of COVID-19.

40. **Prevalence and Impact of Hyponatremia in Patients with Coronavirus Disease 2019 in New York City.** Frontera JA, Valdes E, Huang J, et al. *Crit Care Med.* 2020 Aug 18. doi: 10.1097/CCM.0000000000004605. https://journals.lww.com/ccmjournal/Abstract/9000/Prevalence_and_Impact_of_Hyponatremia_in_Patients.95524.aspx
Findings: Hyponatremia occurred in nearly a third of coronavirus disease 2019 patients, was an independent predictor of in-hospital mortality, and was associated with increased risk of encephalopathy and mechanical ventilation.

41. **Clinicopathological Features and Outcomes of Acute Kidney Injury in Critically Ill COVID-19 with Prolonged Disease Course: A Retrospective Cohort.** Xia P, Wen Y, Duan Y, et al. *J Am Soc Nephrol*. 2020 Aug 21:ASN.2020040426. doi: 10.1681/ASN.2020040426. https://jasn.asnjournals.org/content/early/2020/08/20/ASN.2020040426
Findings: AKI was a common and multifactorial complication in patients critically ill with COVID-19 at the late stage of the disease course. The predominant pathologic finding was acute tubular injury. Older age and higher serum IL-6 level were risk factors of AKI, and KDIGO stage 3 AKI independently predicted death.

42. **The safety of home discharge for low-risk emergency department patients presenting with coronavirus-like symptoms during the COVID-19 pandemic: A retrospective cohort study.** Berdahl CT, Glennon NC, Henreid AJ, Torbati SS. *J Am Coll Emerg Physicians Open.* 2020 Aug 17:10.1002/emp2.12230. doi: 10.1002/emp2.12230. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7436406/
Findings: Of 452 patients, the median age was 38, and 61.7% had no comorbidities. Chest radiographs were performed for 50.4% of patients and showed infiltrates in 14% of those tested. Polymerase chain reaction testing was performed for 28.3% of patients during the index ED visit and was positive in 35.9% of those tested. Follow-up was achieved for 75.4% of patients. ED revisits occurred for 13.7% of patients. The inpatient admission rate at 30 days was 4.6%, with 0.7% requiring intensive care. Median number of days between index ED evaluation and return for admission was 5. There were no known deaths. A minority of low-risk patients with suspected COVID-19 will require hospitalization after being discharged home from the ED. Outpatient management is likely safe for well-appearing patients with normal vital signs, but

patients should be instructed to return for worsening symptoms including labored breathing. Future work is warranted to develop and validate ED disposition guidelines.

Therapeutics

43. **Airway Hygiene in COVID-19 Pneumonia: Treatment Responses of 3 Critically Ill Cruise Ship Employees.** Farooqi FI, Morgan RC, Dhawan N, et al. *Am J Case Rep*. 2020 Aug 18;21:e926596. doi: 10.12659/AJCR.926596. https://www.amjcaserep.com/download/index/idArt/926596
Findings: Three cruise ship employees with COVID-19 underwent endotracheal intubation and were admitted to the ICU for acute hypoxemic respiratory failure. Initial chest X-rays suggested multifocal pneumonia with superimposed ARDS. A regimen of hydroxychloroquine, azithromycin, and dexamethasone was initiated on admission in all cases. Additionally, medications used for pulmonary hygiene were administered through a metered-dose inhaler (MDI) in line with the ventilator circuit. Endotracheal suctioning was performed prior to medication administration. The duration from endotracheal intubation to extubation ranged from 9 to 24 days. All 3 patients reached 30-day survival. The cases reported highlight the importance of the use of airway hygiene with mucolytics, bronchodilators, and tracheal suctioning for patients with COVID-19 pneumonia requiring ventilatory support.

44. **Effectiveness of remdesivir for the treatment of hospitalized Covid-19 persons: a network meta-analysis.** Jiang Y, Chen D, Cai D, Yi Y, Jiang S. *J Med Virol*. 2020 Aug 19. doi: 10.1002/jmv.26443. https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.26443
Findings: Both 10-day and 5-day remdesivir regimens were associated with higher odds of clinical improvement [odds ratio (OR) of 10-day regimen: 1.35, 95% confidence interval (CI): 1.09 - 1.67); OR of 5-day regimen: 1.81, CI: 1.32 - 2.45] and higher probabilities of clinical recovery [relative risk (RR) of 10-day regimen: 1.24, CI: 1.07 - 1.43); RR of 5-day regimen: 1.47, CI: 1.16 - 1.87] compared with placebo. CONCLUSIONS: Remdesivir may have clinical benefits among hospitalized Covid-19 persons.

45. **The impact of sofosbuvir/daclatasvir or ribavirin in patients with severe COVID-19.** Eslami G, Mousaviasl S, Radmanesh E, et al. *J Antimicrob Chemother*. 2020 Aug 19:dkaa331. doi: 10.1093/jac/dkaa331. https://academic.oup.com/jac/advance-article/doi/10.1093/jac/dkaa331/5889946?searchresult=1
Findings: Sixty-two subjects met the inclusion criteria, with 35 enrolled in the sofosbuvir/daclatasvir arm and 27 in the ribavirin arm. The median duration of stay was 5 days for the sofosbuvir/daclatasvir group and 9 days for the ribavirin group. The mortality in the sofosbuvir/daclatasvir group was 2/35 (6%) and 9/27 (33%) for the ribavirin group. The relative risk of death for patients treated with sofosbuvir/daclatasvir was 0.17 and the number needed to treat for benefit was 3.6. CONCLUSIONS: Given these encouraging initial results, and the current lack of treatments proven to decrease mortality in COVID-19, further investigation in larger-scale trials seems warranted.
See also: **Sofosbuvir and daclatasvir compared with standard of care in the treatment of patients admitted to hospital with moderate or severe coronavirus infection**

(COVID-19): a randomized controlled trial. Sadeghi A, Ali Asgari A, Norouzi A, et al. *J Antimicrob Chemother.* 2020 Aug 19:dkaa334. doi: 10.1093/jac/dkaa334.
Evaluation of the efficacy of sofosbuvir plus daclatasvir in combination with ribavirin for hospitalized COVID-19 patients with moderate disease compared with standard care: a single-centre, randomized controlled trial. Abbaspour Kasgari H, Moradi S, Shabani AM, et al. *J Antimicrob Chemother*. 2020 Aug 19:dkaa332. doi: 10.1093/jac/dkaa332.

46. **High-Flow Nasal Oxygen in Coronavirus Disease 2019 Patients with Acute Hypoxemic Respiratory Failure: A Multicenter, Retrospective Cohort Study.** Xia J, Zhang Y, Ni L, et al. *Crit Care Med*. 2020 Aug 19. doi: 10.1097/CCM.0000000000004558.
https://journals.lww.com/ccmjournal/Abstract/9000/High_Flow_Nasal_Oxygen_in_Coronavirus_Disease_2019.95526.aspx
Findings: High-flow nasal oxygen may be effective for treating coronavirus disease 2019 patients with mild to moderate acute hypoxemic respiratory failure. However, high-flow nasal oxygen failure was associated with a poor prognosis. Male and lower oxygenation at admission were the two strong predictors of high-flow nasal oxygen failure.

47. **Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients with Moderate COVID-19: A Randomized Clinical Trial.** Spinner CD, Gottlieb RL, Criner GJ, et al. *JAMA*. 2020 Aug 21. doi: 10.1001/jama.2020.16349.
https://jamanetwork.com/journals/jama/fullarticle/2769871
Findings: Among 596 patients who were randomized, 584 began the study and received remdesivir or continued standard care (median age, 57 [interquartile range, 46-66] years; 227 [39%] women; 56% had cardiovascular disease, 42% hypertension, and 40% diabetes), and 533 (91%) completed the trial. Median length of treatment was 5 days for patients in the 5-day remdesivir group and 6 days for patients in the 10-day remdesivir group. On day 11, patients in the 5-day remdesivir group had statistically significantly higher odds of a better clinical status distribution than those receiving standard care (odds ratio, 1.65; 95% CI, 1.09-2.48; P = .02). The clinical status distribution on day 11 between the 10-day remdesivir and standard care groups was not significantly different (P = .18 by Wilcoxon rank sum test). By day 28, 9 patients had died: 2(1%) in the 5-day remdesivir group, 3 (2%) in the 10-day remdesivir group, and 4 (2%) in the standard care group. Nausea (10% vs 3%), hypokalemia (6% vs 2%), and headache (5% vs 3%) were more frequent among remdesivir-treated patients compared with standard care. CONCLUSIONS: Among patients with moderate COVID-19, those randomized to a 10-day course of remdesivir did not have a statistically significant difference in clinical status compared with standard care at 11 days after initiation of treatment. Patients randomized to a 5-day course of remdesivir had a statistically significant difference in clinical status compared with standard care, but the difference was of uncertain clinical importance.

48. **Empiric Antibacterial Therapy and Community-onset Bacterial Co-infection in Patients Hospitalized with COVID-19: A Multi-Hospital Cohort Study.** Vaughn VM, Gandhi T, Petty LA, et al. *Clin Infect Dis*. 2020 Aug 21:ciaa1239. doi: 10.1093/cid/ciaa1239.
https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1239/5895253

Findings: Of 1705 patients with COVID-19, 56.6% were prescribed early empiric antibacterial therapy; 3.5% (59/1705) had a confirmed community-onset bacterial infection. Across hospitals, early empiric antibacterial use varied from 27%-84%. Patients were more likely to receive early empiric antibacterial therapy if they were older, had a lower body mass index, had more severe illness, had a lobar infiltrate, or were admitted to a for-profit hospital. Over time, COVID-19 test turnaround time and empiric antibacterial use decreased. The prevalence of confirmed community-onset bacterial co-infections was low. Despite this, half of patients received early empiric antibacterial therapy. Antibacterial use varied widely by hospital. Reducing COVID-19 test turnaround time and supporting stewardship could improve antibacterial use.

49. **Tocilizumab and steroid treatment in patients with COVID-19 pneumonia.** Mikulska M, Nicolini LA, Signori A, et al. *PLoS One*. 2020 Aug 20;15(8):e0237831. doi: 10.1371/journal.pone.0237831. eCollection 2020. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0237831
Findings: Overall, 196 adults were included in the analyses. They were mainly male (67.4%), with comorbidities (78.1%) and severe COVID-19 pneumonia (83.7%). Median age was 67.9 years. Among them, 130 received early anti-inflammatory treatment with: tocilizumab (n = 29, 22.3%), methylprednisolone (n = 45, 34.6%), or both (n = 56, 43.1%). The adjusted failure-free survival among tocilizumab/methylprednisolone/SOC treated patients vs. SOC was 80.8% vs. 64.1%. The overall survival among tocilizumab/methylprednisolone/SOC patients vs. SOC was 85.9% vs. 71.9%. Early adjunctive treatment with tocilizumab, methylprednisolone or both may improve outcomes in non-intubated patients with COVID-19 pneumonia.

50. **Use of convalescent plasma in hospitalized patients with COVID-19: case series.** Livia Hegerova, Ted A Gooley, Kelly A Sweerus, Cynthia Maree, Neil Bailey, Megumi Bailey, Vanessa Dunleavy, Krish Patel, Kirsten Alcorn 5, Rebecca Haley 5, Jill M Johnsen 5 6, Barbara A Konkle 5 6, Annamarie C Lahti 7, Morgan L Alexander, Jason D Goldman, Anne Lipke, Sun-Jung Lim, Mark D Sullivan, John S Pauk, John M Pagel [***PSJH authors***] *Blood.* 2020 Aug 6;136(6):759-762. doi: 10.1182/blood.2020006964. https://ashpublications.org/blood/article/136/6/759/461067/Use-of-convalescent-plasma-in-hospitalized
Findings: We report the early clinical experience of 20 hospitalized patients treated with CP compared with 20 matched controls with severe or life-threatening COVID-19 infection. The study suggests that CP use in severe and critically ill patients with COVID-19 may improve survival if given early in the course of disease. The efficacy as a potential therapy needs further study in well-designed trials to better understand the contribution of CP to outcomes in COVID-19.

51. **Tocilizumab among patients with COVID-19 in the intensive care unit: a multicentre observational study.** Biran N, Ip A, Ahn J, et al. *Lancet Rheumatol*. 2020 Aug 14. doi: 10.1016/S2665-9913(20)30277-0. https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30277-0/fulltext
FINDINGS: Between March 1 and April 22, 2020, 764 patients with COVID-19 required support in the ICU, of whom 210 (27%) received tocilizumab. Factors associated with receiving

tocilizumab were patients' age, gender, renal function, and treatment location. 630 patients were included in the propensity score-matched population, of whom 210 received tocilizumab and 420 did not receive tocilizumab. 358 (57%) of 630 patients died, 102 (49%) who received tocilizumab and 256 (61%) who did not receive tocilizumab. Overall median survival from time of admission was not reached among patients receiving tocilizumab and was 19 days (16-26) for those who did not receive tocilizumab. In this observational study, patients with COVID-19 requiring ICU support who received tocilizumab had reduced mortality. Results of ongoing randomised controlled trials are awaited.

Transmission / Infection Control

52. **Novel Insights into the Transmission of SARS-CoV-2 through the Ocular Surface and its Detection in Tears and Conjunctival Secretions: A Review.** Güemes-Villahoz N, Burgos-Blasco B, Vidal-Villegas B, et al. *Adv Ther*. 2020 Aug 18:1-10. doi: 10.1007/s12325-020-01442-7. https://link.springer.com/article/10.1007/s12325-020-01442-7
Findings: This review article critically evaluates available evidence on the ophthalmological mode of viral transmission and the value of earlier identification of the virus on the eye. More evidence is urgently needed to better evaluate the need for protective measures and reliable ocular diagnostic tests to diminish further pandemic spread.

53. **SARS-CoV-2 Infection among Community Health Workers in India Before and After Use of Face Shields.** Bhaskar ME, Arun S. *JAMA*. August 17, 2020. doi:10.1001/jama.2020.15586 https://jamanetwork.com/journals/jama/fullarticle/2769693
Findings: Before face shields, 62 workers (40 women) visited 5880 homes with 31 164 persons. From the 5880 homes visited, 222 persons tested positive for SARS-CoV-2, between May 4 to May 13. Twelve workers (19%) were infected during this period. After face shields, 50 workers (previously uninfected) continued to provide counseling, visiting 18 228 homes. Among the counseled, 118 428 persons, 2682 subsequently tested positive for SARS-CoV-2. No worker developed asymptomatic or symptomatic infection. This study found no SARS-CoV-2 infections among community health workers after the addition of face shields to their personal protective equipment. The face shields may have reduced ocular exposure or contamination of masks or hands or may have diverted movement of air around the face.

54. **Aerosol Generation from the Respiratory Tract with Various Modes of Oxygen Delivery.** Gaeckle NT, Lee J, Park Y, et al. *Am J Respir Crit Care Med*. 2020 Aug 21. doi: 10.1164/rccm.202006-2309OC. https://www.atsjournals.org/doi/pdf/10.1164/rccm.202006-2309OC
Findings: Median particle concentration ranged from 0.041 to 0.168 particles/cm3. Median diameter ranged from 1.01 to 1.53 µm. Cough significantly increased the number of particles measured. Measured aerosol concentration did not significantly increase with the use of either humidified high flow nasal cannula or non-invasive positive pressure ventilation. This was the case during normal breathing, talking, deep breathing, and coughing. Oxygen delivery modalities of humidified high flow nasal cannula and non-invasive positive pressure ventilation

do not increase aerosol generation from the respiratory tract in healthy human participants with no active pulmonary disease measured in a negative pressure room.

55. **Seeding of outbreaks of COVID-19 by contaminated fresh and frozen food.** Fisher D, Reilly A, Kang Eng Zheng A, et al. *bioRxiv PREPRINT*. August 18, 2020 doi: https://doi.org/10.1101/2020.08.17.255166 https://www.biorxiv.org/content/10.1101/2020.08.17.255166v1
Findings: Importation of contaminated food and food packaging is a feasible source for COVID outbreaks and a source of clusters within existing outbreaks. Such events can be prevented if the risk is better appreciated. SARS-CoV-2, can survive on frozen meat and fish for periods up to 3 weeks. We found the presence of infectious (live) virus, not just genetic material, on meat which was previously refrigerated and frozen for up to 3 weeks—and later thawed.

Vaccine

56. **An adenovirus-vectored COVID-19 vaccine confers protection from SARS-COV-2 challenge in rhesus macaques.** Feng L, Wang Q, Shan C, et al. *Nat Commun*. 2020 Aug 21;11(1):4207. doi: 10.1038/s41467-020-18077-5. https://www.nature.com/articles/s41467-020-18077-5
Findings: We report the generation of a replication-incompetent recombinant serotype 5 adenovirus, Ad5-S-nb2, carrying a codon-optimized gene encoding Spike protein (S). In mice and rhesus macaques, intramuscular injection with Ad5-S-nb2 elicits systemic S-specific antibody and cell-mediated immune (CMI) responses. Intranasal inoculation elicits both systemic and pulmonary antibody responses but weaker CMI response. At 30 days after a single vaccination with Ad5-S-nb2 either intramuscularly or intranasally, macaques are protected against SARS-CoV-2 challenge. A subsequent challenge reveals that macaques vaccinated with a 10-fold lower vaccine dosage (1 × 1010 viral particles) are also protected, demonstrating the effectiveness of Ad5-S-nb2 and the possibility of offering more vaccine dosages within a shorter timeframe. Thus, Ad5-S-nb2 is a promising candidate vaccine and warrants further clinical evaluation.

Women & Children

57. **Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women.** Chambers C, Krogstad P, Bertrand K, et al. *JAMA*. August 19, 2020. doi:10.1001/jama.2020.15580 https://jamanetwork.com/journals/jama/fullarticle/2769825
Findings: Of 24 case reports on breast milk samples from women infected with SARS-CoV-2, viral RNA was detected in 10 samples from 4 women.1-6 In some cases, environmental contamination or retrograde flow from an infected infant could not be ruled out. Detection of viral RNA by reverse transcriptase–polymerase chain reaction (RT-PCR) does not equate with infectivity. To date, SARS-CoV-2 has not been isolated from breast milk, and there are no documented cases of transmission of infectious virus to the infant through breast milk. However, potential for viral transmission through breast milk remains a critical question for women infected with SARS-CoV-2 who wish to breastfeed.

58. **Peripheral immunophenotypes in children with multisystem inflammatory syndrome associated with SARS-CoV-2 infection.** Carter MJ, Fish M, Jennings A, et al. *Nat Med.* 2020 Aug 18. doi: 10.1038/s41591-020-1054-6. https://www.nature.com/articles/s41591-020-1054-6 Findings: We performed peripheral leukocyte phenotyping in 25 children with MIS-C, in the acute (n = 23; worst illness within 72 h of admission), resolution (n = 14; clinical improvement) and convalescent (n = 10; first outpatient visit) phases of the illness and used samples from seven age-matched healthy controls for comparisons. Among the MIS-C cohort, 17 (68%) children were SARS-CoV-2 seropositive, suggesting previous SARS-CoV-2 infections14,15, and these children had more severe disease. In the acute phase of MIS-C, we observed high levels of interleukin-1β (IL-1β), IL-6, IL-8, IL-10, IL-17, interferon-γ and differential T and B cell subset lymphopenia. High CD64 expression on neutrophils and monocytes, and high HLA-DR expression on γδ and CD4+CCR7+ T cells in the acute phase, suggested that these immune cell populations were activated. Antigen-presenting cells had low HLA-DR and CD86 expression, potentially indicative of impaired antigen presentation. These features normalized over the resolution and convalescence phases. Overall, MIS-C presents as an immunopathogenic illness1 and appears distinct from Kawasaki disease.

59. **Pediatric SARS-CoV-2: Clinical Presentation, Infectivity, and Immune Responses.** Yonker LM, Neilan AM, Bartsch Y, et al. *J Pediatr*. 2020 Aug 18:S0022-3476(20)31023-4. doi: 10.1016/j.jpeds.2020.08.037. https://www.jpeds.com/article/S0022-3476(20)31023-4/fulltext Findings: A total of 192 children (mean age 10.2 +/- 7 years) were enrolled. Forty-nine children (26%) were diagnosed with acute SARS-CoV-2 infection; an additional 18 children (9%) met criteria for MIS-C. Only 25 (51%) of children with acute SARS-CoV-2 infection presented with fever; symptoms of SARS-CoV-2 infection, if present, were non-specific. Nasopharyngeal viral load was highest in children in the first 2 days of symptoms, significantly higher than hospitalized adults with severe disease (P = .002). Age did not impact viral load, but younger children had lower ACE2 expression (P=0.004). IgM and IgG to the receptor binding domain (RBD) of the SARS-CoV-2 spike protein were increased in severe MIS-C (P<0.001), with dysregulated humoral responses observed. This study reveals that children may be a potential source of contagion in the SARS-CoV-2 pandemic in spite of milder disease or lack of symptoms, and immune dysregulation is implicated in severe post-infectious MIS-C.

60. **Limited Secondary Transmission of SARS-CoV-2 in Child Care Programs — Rhode Island, June 1–July 31, 2020.** Link-Gelles R, DellaGrotta AL, Molina C, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 21 August 2020. DOI: http://dx.doi.org/10.15585/mmwr.mm6934e2 https://www.cdc.gov/mmwr/volumes/69/wr/mm6934e2.htm?s_cid=mm6934e2_x Findings: On June 1, 2020, child care programs in the state reopened after a nearly 3-month closure. To reopen safely, the Rhode Island Department of Human Services required licensed center- and home-based child care programs to reduce enrollment, initially to a maximum of 12 persons, including staff members, in stable groups (i.e., staff members and students not switching between groups) in physically separated spaces, increasing to a maximum of 20 persons on June 29. Additional requirements included universal use of masks for adults, daily symptom screening of adults and children, and enhanced cleaning and disinfection according to CDC guidelines. As of July 31, 75% of programs were approved to reopen, with capacity for

18,945 children, representing 74% of the state's January 2020 child care program population (25,749 children). A total of 101 possible child care–associated COVID-19 cases were reported during June 1–July 31. Cases occurred in 29 child care programs, 20 (69%) of which had a single case with no apparent secondary transmission. Five (15%) programs had two to five cases.

GUIDELINES & CONSENSUS STATEMENTS

Multidisciplinary Guidance Regarding the Use of Immunomodulatory Therapies for Acute COVID-19 in Pediatric Patients. Dulek DE, Fuhlbrigge RC, Tribble AC, et al. *J Pediatric Infect Dis Soc.* 2020 Aug 18:piaa098. doi: 10.1093/jpids/piaa098.

Management strategies for children with COVID-19: ESPR practical recommendations. Raissaki M, Shelmerdine SC, Damasio MB, et al. *Pediatr Radiol.* 2020 Aug;50(9):1313-1323. doi: 10.1007/s00247-020-04749-3.

Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19: Serologic Testing.

FDA / CDC / NIH / WHO Updates

CDC - **Interim Additional Guidance for Infection Prevention and Control Recommendations for Patients with Suspected or Confirmed COVID-19 in Outpatient Hemodialysis Facilities.** Updated 8/23/20

CDC - **COVID-19 Response Health Equity Strategy: Accelerating Progress Towards Reducing COVID-19 Disparities and Achieving Health Equity.**

FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID–19 Treatment, Another Achievement in Administration's Fight Against Pandemic. August 23, 2020

WHO - **Advice on the use of masks for children in the community in the context of COVID-19.**

WHO - **Considerations for quarantine of contacts of COVID-19 cases, Interim guidance.**

Commentary / News

Building a Better Health Care System Post-Covid-19: Steps for Reducing Low-Value and Wasteful Care.

Millions of students are returning to US universities in a vast unplanned pandemic experiment.

Behavioural manipulation - key to the successful global spread of the new Coronavirus SARS-Cov-2? Bouayed J, Bohn T. *J Med Virol*. 2020 Aug 19. doi: 10.1002/jmv.26446.

*First Documented Coronavirus Reinfection Reported in Hong Kong. NY Times, August 24, 2020. See study details under *Epidemiology* section above.

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**

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