Providence

COVID-19 Resource Desk

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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. **A review on drug repurposing applicable to COVID-19.** Dotolo S, Marabotti A, Facchiano A, et al. *Brief Bioinform.* 2020 Nov 5;bbaa288. doi: 10.1093/bib/bbaa288. https://academic.oup.com/bib/advance-article/doi/10.1093/bib/bbaa288/5956159
Findings: Drug repurposing involves the identification of new applications for existing drugs at a lower cost and in a shorter time. There are different computational drug-repurposing strategies and some of these approaches have been applied to the coronavirus disease 2019 (COVID-19) pandemic. Computational drug-repositioning approaches applied to COVID-19 can be broadly categorized into (i) network-based models, (ii) structure-based approaches and (iii) artificial intelligence (AI) approaches. Network-based approaches are divided into two categories: network-based clustering approaches and network-based propagation approaches. Both of them allowed to annotate some important patterns, to identify proteins that are functionally associated with COVID-19 and to discover novel drug-disease or drug-target relationships useful for new therapies. Structure-based approaches allowed to identify small chemical compounds able to bind macromolecular targets to evaluate how a chemical compound can interact with the biological counterpart, trying to find new applications for existing drugs. AI-based networks appear, at the moment, less relevant since they need more data for their application.

2. **Effect and Reach of Medical Articles Posted on Preprint Servers During the COVID-19 Pandemic.** Jung Y, Sun Y, Schluger NW. *JAMA Intern Med.* November 9, 2020. doi:10.1001/jamainternmed.2020.6629 https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2772329?resultClick=1
Findings: In a small study comparing articles about therapies for COVID-19 posted on the medRxiv preprint server, subsequent publications in medical journals of some of these articles, and journal articles that were not posted on either medRxiv or another preprint server, we found widespread dissemination of reports that had not undergone traditional peer review. We also found that articles posted as preprints but that were not published during the study period received less attention that those that did across multiple metrics.

3. **Variant analysis of 1,040 SARS-CoV-2 genomes.** Rouchka EC, Chariker JH, Chung D. *PLoS One.* 2020 Nov 5;15(11):e0241535. doi: 10.1371/journal.pone.0241535. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0241535
Findings: The SARS-CoV-2 viral genome is an RNA virus consisting of approximately 30,000 bases. As part of testing efforts, whole genome sequencing of human isolates has resulted in over 1,600 complete genomes publicly available from GenBank. We have performed a comparative analysis of the sequences, in order to detect common mutations within the population. Analysis of variants occurring within the assembled genomes yields 417 variants occurring in at least 1% of the completed genomes, including 229 within the 5' untranslated region (UTR), 152 within the 3'UTR, 2 within intergenic regions and 34 within coding sequences.

Clinical Syndrome

4. **Clinical Characteristics and Outcomes of Non-ICU Hospitalization for COVID-19 in a Nonepicenter, Centrally Monitored Healthcare System.** Nemer DM, Wilner BR, Burkle A, et al. *J Hosp Med.* 2020 Oct 21. doi: 10.12788/jhm.3510. https://www.journalofhospitalmedicine.com/jhospmed/original-research
Findings: Systematic analysis of all non-ICU patient hospitalizations for COVID-19 completing discharge between March 13 and May 1, 2020, in a large US health care system utilizing off-site central monitoring. Among 350 patients (age, 64 ± 16 years; 55% male), most (73%) required 3 L/min or less of supplemental oxygen during admission. Telemetry was widely utilized (79%) yet arrhythmias were uncommon (14%) and were predominantly (90%) among patients with abnormal troponin levels or known cardiovascular disease. Ventricular tachycardia was rare (5%), nonsustained, and not associated with hydroxychloroquine/azithromycin treatment. Adverse events occurred in 62 patients (18%), including 22 deaths (6%), 48 ICU transfers (14%), and 49 patients with increased oxygen requirement (14%) and were independently associated with elevated C-reactive protein and lactate dehydrogenase in multivariable analysis. Among non-critically ill patients hospitalized within a nonepicenter health care system, overall survival was 94% with the development of more severe illness or death independently associated with higher levels of C-reactive protein and lactate dehydrogenase on admission.

5. **Evidence of systemic endothelial injury and microthrombosis in hospitalized COVID-19 patients at different stages of the disease.** Della Rocca DG, Magnocavallo M, Lavalle C, et al. *J Thromb Thrombolysis.* 2020 Nov 6. doi: 10.1007/s11239-020-02330-1. https://link.springer.com/article/10.1007/s11239-020-02330-1
Findings: Schistocytes are fragments of red blood cells which may be encountered in the peripheral blood smear of patients suffering from a variety of microangiopathic diseases. In the hospitalized COVID-19 patients at different stages of disease severity, a schistocyte count ≥ 1% was documented in approximately 70% of patients. Evidence of myocardial injury was observed in 87.5% of all who had a count of schistocytes ≥ 1%. Schistocytes may serve as a simple and inexpensive biomarker to identify a high-risk subpopulation with a latent systemic microvascular damage irrespective of respiratory symptoms.

6. **Characteristics and outcomes of COVID-19-associated stroke: a UK multicentre case-control study.** SETICOS collaborators. *J Neurol Neurosurg Psychiatry*. 2020 Nov 5:jnnp-2020-324927. doi: 10.1136/jnnp-2020-324927. https://jnnp.bmj.com/content/jnnp/early/2020/11/03/jnnp-2020-324927.full.pdf
   Findings: Cases with ischaemic stroke were more likely than ischaemic controls to occur in Asians (18.8% vs 6.7%, p<0.0002), were more likely to involve multiple large vessel occlusions (17·9% vs 8.1%, p<0·03), were more severe (median NIHSS 8 vs 5, p<0·002), were associated with higher D-dimer levels (p<0·01) and were associated withmore severe disability on discharge (median mRS 4 vs 3, p<0·0001) and inpatientdeath (19.8% vs9·6%, p<0·0001). Recurrence of stroke during the patient's admission was rare in Cases and Controls (2.3% vs1.0%, NS). Our data suggest that COVID-19 may be an important modifier of the onset, characteristics and outcome of acute ischaemic stroke.

7. **Dermatologic manifestations of COVID-19: a comprehensive systematic review.** Mirza FN, Malik AA, Omer SB, Sethi A. *Int J Dermatol.* 2020 Nov 3. doi: 10.1111/ijd.15168. https://onlinelibrary.wiley.com/doi/abs/10.1111/ijd.15168
   Findings: From 86 retrieved studies, we collated data on 2,560 patients with dermatologic manifestations of COVID-19. The most common findings were chilblains/pernio-like lesion (51.5%), erythematous maculopapular rashes (13.3%), and viral exanthem (7.7%). Average pediatric age was 12.9 years (SD 3.6) and adult was 34.2 years (SD 21.8). Average latency from time of upper respiratory illness symptoms to cutaneous findings was 1.5 days in children and 7.9 days in adults, ranging from -3 to 38 days. Roughly one-tenth in both populations were otherwise asymptomatic or presented with only skin findings for the entirety of the disease course; 13.3% (pediatrics) and 5.3% (adults) presented with skin issues first. Dermatologic findings may play an important role in identifying cases early and serve as an important proxy to manage spread. Further prospective data collection with international prospective registries is needed.

8. **Characteristics of Hospitalized COVID-19 Patients Discharged and Experiencing Same-Hospital Readmission — United States, March–August 2020.** Lavery AM, Preston LE, Ko JY, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 9 November 2020. DOI: http://dx.doi.org/10.15585/mmwr.mm6945e2
   Findings: Evidence suggests that potential health complications after COVID-19 illness might require ongoing clinical care. After discharge from an initial COVID-19 hospitalization, 9% of patients were readmitted to the same hospital within 2 months of discharge. Multiple readmissions occurred in 1.6% of patients. Risk factors for readmission included age ≥65 years, presence of certain chronic conditions, hospitalization within the 3 months preceding the first COVID-19 hospitalization, and discharge to a skilled nursing facility or with home health care. Understanding frequency of, and potential reasons for, readmission after a COVID-19 hospitalization can inform clinical practice, discharge disposition decisions, and public health priorities, such as health care resource planning.

Diagnostics & Screening

9. **Boosting test-efficiency by pooled testing for SARS-CoV-2-Formula for optimal pool size.** Hanel R, Thurner S. *PLoS One.* 2020 Nov 4;15(11):e0240652. doi: 10.1371/journal.pone.0240652. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0240652
Findings: For low overall infection levels in the population the pooling of samples can drastically amplify the testing capacity. Here we present a formula to estimate the optimal group-size for pooling, the efficiency gain (tested persons per test), and the expected upper bound of missed infections in pooled testing, all as a function of the population-wide infection levels and the false negative/positive rates of the currently used PCR tests. Assuming an infection level of 0.1% and a false negative rate of 2%, the optimal pool-size is about 34, and an efficiency gain of about 15 tested persons per test is possible. For an infection level of 1% the optimal pool-size is 11, the efficiency gain is 5.1 tested persons per test. For an infection level of 10% the optimal pool-size reduces to about 4, the efficiency gain is about 1.7 tested persons per test. For infection levels of 30% and higher there is no more benefit from pooling.

10. **Repeated cross-sectional sero-monitoring of SARS-CoV-2 in New York City.** Stadlbauer D, Tan J, Jiang K, et al. *Nature.* 2020 Nov 3. doi: 10.1038/s41586-020-2912-6. https://www.nature.com/articles/s41586-020-2912-6
Findings: The first COVID-19 case in NYC was officially confirmed on March 1st 2020 followed by a severe local epidemic. To understand seroprevalence dynamics, we conducted a retrospective, repeated cross-sectional analysis of anti-SARS-CoV-2 spike antibodies in weekly intervals from the beginning of February to July 2020 using more than 10,000 plasma samples from patients at Mount Sinai Hospital in NYC. Here we show the dynamics of seroprevalence in an 'urgent care' (UC) group, enriched for COVID-19 cases during the epidemic, and a 'routine care' group (RC), which more closely represents the general population. Seroprevalence increased at different rates in both groups, with seropositive samples as early as mid-February, and levelled out at slightly above 20% in both groups after the epidemic wave subsided by the end of May. From May to July seroprevalence stayed stable, suggesting lasting antibody levels in the population. Our data suggest an earlier than previously documented introduction of SARS-CoV-2 into NYC and describe the dynamics of seroconversion over the full course of the first pandemic wave in a major metropolitan area.

Epidemiology & Public Health

11. **Public perceptions of the effectiveness of recommended non-pharmaceutical intervention behaviors to mitigate the spread of SARS-CoV-2.** Kasting ML, Head KJ, Hartsock JA, et al. *PLoS One.* 2020 Nov 4;15(11):e0241662. doi: 10.1371/journal.pone.0241662. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0241662
Findings: In May 2020, we conducted a cross-sectional survey among U.S. adults (N = 3,474). The primary outcome was a six-item measure assessing perceived effectiveness of recommended behaviors to prevent SARS-CoV-2 infection from 1 (not at all effective) to 5 (extremely effective). The sample was divided into "higher" and "lower" perceived effectiveness

groups. Mean age was 45.5 years and most participants were non-Hispanic White (63%) and female (52.4%). COVID-19-related worry and perceived threat to physical health were positively associated with perceived effectiveness while perceived severity of COVID-19 and perceived likelihood of infection switched directions in the adjusted model and were negatively associated with perceived effectiveness. This research indicates people generally believe NPI are effective, but there was variability based on health beliefs and there are mixed rates of engagement in these behaviors. Public health efforts should focus on increasing perceived severity and threat of SARS-CoV-2-related disease, while promoting NPI as effective in reducing threat.

12. **A Risk Model of Admitting Patients with Silent SARS-CoV-2 Infection to Surgery and Development of Severe Postoperative Outcomes and Death: Projections Over 24 Months for 5 Geographical Regions.** Soreide K, Yaqub S, Hallet J, et al. *Ann Surg*. 2020 Nov 4. doi: 10.1097/SLA.0000000000004583. https://europepmc.org/article/med/33156071
Findings: We developed two sets of models to evaluate the risk of admitting silent COVID-19-infected patients to surgery. A static model let the underlying infection rate and the gross population-rate of surgery vary. In a stochastic model, the dynamics of the COVID-19 prevalence and a fixed population-rate of surgery was considered. We generated uncertainty intervals (UIs) for our estimates by running low and high scenarios using the lower and upper 90% uncertainty limits. Both models provided concerning rates of perioperative risk over a 24-months period. For the US, the modelled rates were 92·000 pulmonary complications and almost 30·000 deaths, respectively; for Europe, some 131·000 patients with pulmonary complications and close to 47·000 deaths were modelled. The model highlights a considerable risk of admitting patients with silent COVID-19 to surgery with an associated risk for adverse perioperative outcomes and deaths. Strategies to avoid excessive complications and deaths after surgery during the pandemic are needed.

13. **Risk of Severe COVID-19 among Workers and Their Household Members.** Selden TM, Berdahl TA *JAMA Intern Med.* November 9, 2020. doi:10.1001/jamainternmed.2020.6249
https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2772328?resultClick=1
Findings: Between 56.7 and 74.3 million increased-risk US adults lived with or were themselves essential workers who could not work at home (WAH). These estimates were driven by 3 factors: First, 49.7% to 61.0% of all adults were at increased risk of severe COVID-19 if infected with SARS-CoV-2 (depending on the CDC definition used). Second, 71.5% of workers held essential jobs, and many were unable to WAH. Third, we measured not only the number of adults with increased risk who were essential workers and unable to WAH, but also the many increased-risk adults living with such workers. One limitation is that the study's prepandemic data do not reflect current employment levels, changes in ability to WAH, or local infection rates. Additionally, risk factors were reported by MEPS participants rather than measured by medical professionals, likely causing an underestimate of risk. Policy makers seeking to make efficient and equitable decisions about reopening the economy and about vaccine distribution should consider the health risks not only of workers, but also of those with whom they live.

14. **Telework before Illness Onset Among Symptomatic Adults Aged ≥18 Years with and Without COVID-19 in 11 Outpatient Health Care Facilities — United States, July 2020.** Fisher KA, Olson SM, Tenforde MW, et al. *MMWR Morb Mortal Wkly Rep* 2020;69:1648–1653. DOI: http://dx.doi.org/10.15585/mmwr.mm6944a4
    Findings: Since March 2020, large scale measures to reduce workplace transmission of SARS-CoV-2, including workplace closures and providing telework options, have been implemented. Adults who received positive test results for SARS-CoV-2 infection were more likely to report exclusively going to an office or school setting in the 2 weeks before illness onset, compared with those who tested negative, even among those working in a profession outside of the critical infrastructure. Businesses and employers should promote alternative work site options, such as teleworking, where possible, to reduce exposures to SARS-CoV-2. Where telework options are not feasible, worker safety measures should continue to be scaled up to reduce possible worksite exposures.

Healthcare Delivery & Healthcare Workers

15. **Interventions to support the resilience and mental health of frontline health and social care professionals during and after a disease outbreak, epidemic or pandemic: a mixed methods systematic review.** *Cochrane Database Syst Rev.* 2020 Nov 5;11:CD013779. doi: 10.1002/14651858.CD013779.
    https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013779/full
    Findings: There is a lack of both quantitative and qualitative evidence from studies carried out during or after disease epidemics and pandemics that can inform the selection of interventions that are beneficial to the resilience and mental health of frontline workers. Alternative sources of evidence (e.g. from other healthcare crises, and general evidence about interventions that support mental well-being) could therefore be used to inform decision making. When selecting interventions aimed at supporting frontline workers' mental health, organisational, social, personal, and psychological factors may all be important. Research to determine the effectiveness of interventions is a high priority. The COVID-19 pandemic provides unique opportunities for robust evaluation of interventions. Future studies must be developed with appropriately rigorous planning, including development, peer review and transparent reporting of research protocols, following guidance and standards for best practice, and with appropriate length of follow-up. Factors that may act as barriers and facilitators to implementation of interventions should be considered during the planning of future research and when selecting interventions to deliver within local settings.

16. **COVID-19 seropositivity and asymptomatic rates in healthcare workers are associated with job function and masking.** Sims MD, Maine GN, Childers KL, et al. *Clin Infect Dis*. 2020 Nov 5:ciaa1684. doi: 10.1093/cid/ciaa1684. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1684/5956266
    Findings: A total of 1,818 (8.8%) participants were seropositive between April 13 and May 28, 2020. Among the seropositive individuals, 44% reported that they were asymptomatic during the month prior to blood collection. Healthcare roles such as phlebotomy, respiratory therapy, and nursing/nursing support exhibited significantly higher seropositivity. Among participants

reporting direct exposure to a COVID-19 positive individual, those wearing an N95/PAPR mask had a significantly lower seropositivity rate (10.2%) compared to surgical/other masks (13.1%) or no mask (17.5%). Direct contact with COVID-19 patients increased the likelihood of seropositivity among employees but study participants who wore a mask during COVID-19 exposures were less likely to be seropositive. Additionally, a large proportion of seropositive employees self-reported as asymptomatic.

17. **US Clinicians' Experiences and Perspectives on Resource Limitation and Patient Care During the COVID-19 Pandemic.** Butler CR, Wong SPY, Wightman AG, et al. *JAMA Netw Open*. 2020;3(11):e2027315. doi:10.1001/jamanetworkopen.2020.27315
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2772567?resultClick=3
Findings: Little is known about how US clinicians have responded to resource limitation during the COVID-19 pandemic. The 61 participants (mean age, 46 years; 38 [63%] women) included in this study were practicing in 15 US states and were more heavily sampled from areas with the highest rates of COVID-19 infection at the time of interviews. Most participants were White individuals (39 [65%]), were attending physicians (45 [75%]), and were practicing in large academic centers (≥300 beds, 51 [85%]; academic centers, 46 [77%]). Three overlapping and interrelated themes emerged from qualitative analysis, as follows: (1) planning for crisis capacity, (2) adapting to resource limitation, and (3) multiple unprecedented barriers to care delivery. Clinician leaders worked within their institutions to plan a systematic approach for fair allocation of limited resources in crisis settings so that frontline clinicians would not have to make rationing decisions at the bedside. However, even before a declaration of crisis capacity, clinicians encountered varied and sometimes unanticipated forms of resource limitation that could compromise care, require that they make difficult allocation decisions, and contribute to moral distress. Furthermore, unprecedented challenges to caring for patients during the pandemic, including the need to limit in-person interactions, the rapid pace of change, and the dearth of scientific evidence, added to the challenges of caring for patients and communicating with families.

18. **Implications of Early Health Care Spending Reductions for Expected Spending as the COVID-19 Pandemic Evolves.** McWilliams JM, Mehrotra A, Russo A. *JAMA Intern Med*. 2020 Nov 9. doi: 10.1001/jamainternmed.2020.5333.
https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2772327
Findings: The early phase of the COVID-19 pandemic was associated with a massive decrease in medical spending for the privately insured. Areas with higher COVID-19 activity had larger spending reductions, as increases in COVID-19 spending were more than offset by decreases in spending on non–COVID-19 care. Spending reductions in high-activity states were similarly substantial for seniors, who are at greater risk of hospitalization for COVID-19. Findings for low-activity states suggest a relationship between elevated concern for viral transmission (manifest as earlier distancing policies) and lower use of medical care. As cases surge in new areas and concerns about transmission prompt states to reimpose restrictions, these findings suggest that health care spending will likely rise and fall inversely with the severity of the pandemic and remain below prepandemic levels for its duration.

Laboratory Results

19. **Lack of antibodies to SARS-CoV-2 in a large cohort of previously infected persons.** Petersen LR, Sami S, Vuong N, et al. *Clin Infect Dis*. 2020 Nov 4;ciaa1685. doi: 10.1093/cid/ciaa1685. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1685/5956137
Findings: We analyzed serologic data collected from health care workers and first responders in New York City and the Detroit metropolitan area with history of a positive SARS-CoV-2 RT-PCR test result and who were tested for IgG antibodies to SARS-CoV-2 spike protein at least 2 weeks after symptom onset. Of 2,547 persons with previous confirmed SARS-CoV-2 infection, 160 (6.3%) were seronegative. Of 2,112 previously symptomatic persons, the proportion seronegative slightly increased from 14 to 90 days post symptom onset. Persons taking immunosuppressive medications were more likely to be seronegative, while participants of non-Hispanic Black race/ethnicity (versus non-Hispanic White), with severe obesity, or with more symptoms were less likely to be seronegative. In our population with previous RT-PCR confirmed infection, approximately one in 16 persons lacked IgG antibodies. Absence of antibodies varied independently by illness severity, race/ethnicity, obesity, and immunosuppressive drug therapy.

20. **Preexisting and de novo humoral immunity to SARS-CoV-2 in humans.** Ng KW, Faulkner N, Cornish GH, et al. *Science*. 2020 Nov 6:eabe1107. doi: 10.1126/science.abe1107. https://science.sciencemag.org/content/early/2020/11/05/science.abe1107
Findings: Zoonotic introduction of novel coronaviruses may encounter preexisting immunity in humans. Using diverse assays for antibodies recognizing SARS-CoV-2 proteins, we detect preexisting humoral immunity. SARS-CoV-2 spike glycoprotein (S)-reactive antibodies were detectable by a flow cytometry-based method in SARS-CoV-2-uninfected individuals and were particularly prevalent in children and adolescents. They were predominantly of the IgG class and targeted the S2 subunit. By contrast, SARS-CoV-2 infection induced higher titers of SARS-CoV-2 S-reactive IgG antibodies, targeting both the S1 and S2 subunits, and concomitant IgM and IgA antibodies, lasting throughout the observation period. Notably, SARS-CoV-2-uninfected donor sera exhibited specific neutralizing activity against SARS-CoV-2 and SARS-CoV-2 S pseudotypes. Distinguishing preexisting and de novo immunity will be critical for our understanding of susceptibility to and the natural course of SARS-CoV-2 infection.

    *see also, **High prevalence of pre-existing serological cross-reactivity against SARS-CoV-2 in sub-Sahara Africa.** *Int J Infect Dis.* November 07, 2020 DOI:https://doi.org/10.1016/j.ijid.2020.10.104

Prognosis

21. **Characteristics and Outcomes of Patients 80 Years and Older Hospitalized with Coronavirus Disease 2019 (COVID-19).** Nabors C, Sridhar A, Hooda U, et al. *Cardiol Rev*. 2020 Nov 4. doi: 10.1097/CRD.0000000000000368. https://journals.lww.com/cardiologyinreview/Abstract/9000/Characteristics_and_Outcomes_of_Patients_80_Years.99617.aspx

Findings: We characterize the clinical course and outcomes of 73 patients aged 80 or older hospitalized at an academic center between March 15th and May 13th, 2020. These patients had multiple comorbidities and often presented with atypical clinical findings such as altered sensorium, generalized weakness and falls. Cardiovascular manifestations observed at the time of presentation included new arrhythmia 7/73 (10%), stroke/intracranial hemorrhage 5/73 (7%) and elevated troponin 27/58 (47%). During hospitalization, 38% of all patients required intensive care, 13% developed a need for renal replacement therapy and 32% required vasopressor support. All-cause mortality was 47% and was highest in patients who were ever in intensive care (71%), required mechanical ventilation (83%), or vasopressors (91%), or developed a need for renal replacement therapy (100%). Patients older than 80 years old with COVID-19 have multiple unique risk factors which can be associated with increased cardiovascular involvement and death.

22. **Is older age associated with COVID-19 mortality in the absence of other risk factors? General population cohort study of 470,034 participants.** Ho FK, Petermann-Rocha F, Gray SR, et al. *PLoS One.* 2020 Nov 5;15(11):e0241824. doi: 10.1371/journal.pone.0241824
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0241824
Findings: Among eligible participants, 438 (0.09%) died of COVID-19. Current age was associated exponentially with COVID-19 mortality. Overall, participants aged ≥75 years were at 13-fold mortality risk compared with those <65 years. Low forced expiratory volume in 1 second, high systolic blood pressure, low handgrip strength, and multiple long-term conditions were significant mediators, and collectively explained 39.3% of their excess risk. The associations between these risk factors and COVID-19 mortality were stronger among older participants. Participants aged ≥75 without additional risk factors were at 4-fold risk compared with all participants aged <65 years. Higher COVID-19 mortality among older adults was partially explained by other risk factors. 'Healthy' older adults were at much lower risk. Nonetheless, older age was an independent risk factor for COVID-19 mortality.

23. **Outcomes of COVID-19 in Patients with a History of Cancer and Comorbid Cardiovascular Disease.** Ganatra S, Dani SS, Redd R, et al. *J Natl Compr Canc Netw.* 2020 Nov 3:1-10. doi: 10.6004/jnccn.2020.7658.
Findings: This retrospective study included 2,476 patients who tested positive for SARS-CoV-2 at 4 Massachusetts hospitals between March 11 and May 21, 2020. Patients were stratified by a history of either cancer (n=195) or CVD (n=414) and subsequently by the presence of both cancer and CVD (n=82). Patients with a history of both cancer and CVD are at significantly higher risk of experiencing COVID-19-associated adverse outcomes. Aggressive public health measures are needed to mitigate the risks of COVID-19 infection in this vulnerable patient population.

24. **COVID-19 Hospitalization in Adults with Type 1 Diabetes: Results from the T1D Exchange Multi-Center Surveillance Study.** O'Malley G, Ebekozien O, Desimone M, et al. *J Clin Endocrinol Metab.* 2020 Nov 9:dgaa825. doi: 10.1210/clinem/dgaa825.
https://academic.oup.com/jcem/advance-article/doi/10.1210/clinem/dgaa825/5963916

Findings: A total of 113 cases were analyzed. Fifty-eight patients were hospitalized, and five patients died. Patients who were hospitalized were more likely to be older, to identify as non-Hispanic Black, to use public insurance, or to have hypertension, and less likely to use continuous glucose monitoring or insulin pumps. Median HbA1c was 8.6% (70 mmol/mol) and was positively associated with hospitalization (OR 1.42, 95% CI 1.18-1.76), which persisted after adjustment for age, sex, race, and obesity. Baseline glycemic control and access to care are important modifiable risk factors which need to be addressed to optimize care of people with type 1 diabetes during the worldwide COVID-19 pandemic.

Survivorship & Rehabilitation

25. **A clinic blueprint for post-COVID-19 RECOVERY: Learning from the past, looking to the future.** Lutchmansingh DD, Knauert MP, Antin-Ozerkis DE, et al. *Chest*. 2020 Nov 4:S0012-3692(20)35125-4. doi: 10.1016/j.chest.2020.10.067. https://www.sciencedirect.com/science/article/abs/pii/S0012369220351254
Findings: The creation of multidisciplinary post-COVID-19 clinics to address both persistent symptoms and potential long-term complications requires an understanding of the acute disease and the emerging data regarding COVID-19 outcomes. Experience with severe acute respiratory syndrome and Middle East respiratory syndrome, post-acute respiratory distress syndrome complications, and post-intensive care syndrome also informs anticipated sequelae and clinical program design. Post-COVID-19 clinical programs should be prepared to care for individuals previously hospitalized with COVID-19 (including those who required critical care support), non-hospitalized individuals with persistent respiratory symptoms following COVID-19 infection, and individuals with pre-existing lung disease complicated by COVID-19. Effective multidisciplinary collaboration models leverage lessons learned during the early phases of the pandemic to overcome the unique logistical challenges posed by pandemic circumstances. Collaboration between clinicians and researchers across disciplines will provide insight into survivorship that may shape the treatment of both acute disease and chronic complications. In this review, we discuss the aims, general principles, elements of design, and challenges of a successful multidisciplinary model to address the needs of COVID-19 survivors.

26. **Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA.** Taquet M, Luciano S, Geddes JR, et al. *Lancet Psychiatry.* November 09, 2020DOI: https://doi.org/10.1016/S2215-0366(20)30462-4
Findings: Adverse mental health consequences of COVID-19, including anxiety and depression, have been widely predicted but not yet accurately measured. There are a range of physical health risk factors for COVID-19, but it is not known if there are also psychiatric risk factors. In this electronic health record network cohort study using data from 69 million individuals, 62 354 of whom had a diagnosis of COVID-19, we assessed whether a diagnosis of COVID-19 (compared with other health events) was associated with increased rates of subsequent psychiatric diagnoses, and whether patients with a history of psychiatric illness are at a higher risk of being diagnosed with COVID-19. In patients with no previous psychiatric history, a diagnosis of COVID-19 was associated with increased incidence of a first psychiatric diagnosis in the following 14 to 90 days compared with six other health events (HR 2·1, 95% CI 1·8–2·5 vs

influenza; 1·7, 1·5–1·9 vs other respiratory tract infections; 1·6, 1·4–1·9 vs skin infection; 1·6, 1·3–1·9 vs cholelithiasis; 2·2, 1·9–2·6 vs urolithiasis, and 2·1, 1·9–2·5 vs fracture of a large bone). The HR was greatest for anxiety disorders, insomnia, and dementia. Survivors of COVID-19 appear to be at increased risk of psychiatric sequelae, and a psychiatric diagnosis might be an independent risk factor for COVID-19. Although preliminary, our findings have implications for clinical services, and prospective cohort studies are warranted.

27. **Persistent fatigue following SARS-CoV-2 infection is common and independent of severity of initial infection.** Townsend L, Dyer AH, Jones K, et al. *PLoS One*. 2020 Nov 9;15(11):e0240784. doi: 10.1371/journal.pone.0240784.
https://journals.plos.org/plosone/article/comments?id=10.1371/journal.pone.0240784
Findings: We examined the prevalence of fatigue in individuals recovered from the acute phase of COVID-19 illness using the Chalder Fatigue Score (CFQ-11). We further examined potential predictors of fatigue following COVID-19 infection, evaluating indicators of COVID-19 severity, markers of peripheral immune activation and circulating pro-inflammatory cytokines. Of 128 participants (49.5 ± 15 years; 54% female), more than half reported persistent fatigue (67/128; 52.3%) at median of 10 weeks after initial COVID-19 symptoms. There was no association between COVID-19 severity (need for inpatient admission, supplemental oxygen or critical care) and fatigue following COVID-19. Additionally, there was no association between routine laboratory markers of inflammation and cell turnover (leukocyte, neutrophil or lymphocyte counts, neutrophil-to-lymphocyte ratio, lactate dehydrogenase, C-reactive protein) or pro-inflammatory molecules (IL-6 or sCD25) and fatigue post COVID-19. Female gender and those with a pre-existing diagnosis of depression/anxiety were over-represented in those with fatigue. Our findings demonstrate a significant burden of post-viral fatigue in individuals with previous SARS-CoV-2 infection after the acute phase of COVID-19 illness. This study highlights the importance of assessing those recovering from COVID-19 for symptoms of severe fatigue, irrespective of severity of initial illness, and may identify a group worthy of further study and early intervention.

Therapeutics

28. **Effect of Hydroxychloroquine on Clinical Status at 14 Days in Hospitalized Patients With COVID-19 A Randomized Clinical Trial.** Self WH, Semler MW, Leither LM, et al. *JAMA*. November 9, 2020. doi:10.1001/jama.2020.22240
https://jamanetwork.com/journals/jama/fullarticle/2772922?resultClick=1
Findings: In this randomized clinical trial that included 479 hospitalized adults with respiratory symptoms from COVID-19, the distribution of the day 14 clinical status score (measured using a 7-category ordinal scale) was not significantly different for patients randomized to receive hydroxychloroquine compared with placebo (adjusted odds ratio, 1.02). These findings do not support the use of hydroxychloroquine for treatment of COVID-19 among hospitalized adults.

29. **The Cardiac Toxicity of Chloroquine or Hydroxychloroquine in COVID-19 Patients: A Systematic Review and Meta-regression Analysis.** Tleyjeh IM, Kashour Z, AlDosary O, et al.

Mayo Clin Proc Innov Qual Outcomes. 2020 Nov 2. doi: 10.1016/j.mayocpiqo.2020.10.005. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7605861/
Findings: A total of 19 studies with a total of 5652 patients were included. The pooled incidence of TdP arrhythmia or VT or cardiac arrest was 3 per 1000, 95% CI (0-21), I2=96%, 18 studies with 3725 patients. Among 13 studies of 4334 patients, the pooled incidence of discontinuation of CQ or HCQ due to prolonged QTc or arrhythmias was 5%, 95% CI (1-11), I2=98%. The pooled incidence of change in QTc from baseline of ≥ 60 ms or QTc ≥ 500 ms was 9%, 95% CI (3-17), I2=97%. Mean/median age, coronary artery disease, hypertension, diabetes, concomitant QT prolonging medications, ICU care, and severity of illness in the study populations explained between-studies heterogeneity. Treatment of COVID-19 patients with CQ or HCQ is associated with a significant risk of drug-induced QT prolongation and relatively higher incidence of TdP/VT/cardiac arrest. Therefore, these agents should not be used routinely in the management of COVID-19 disease. COVID-19 patients who are treated with antimalarials for other indications should be adequately monitored.

30. **Pharmacotherapy for Hospitalized Patients with COVID-19: Treatment Patterns by Disease Severity.** Lin KJ, Schneeweiss S, Tesfaye H, et al. *Drugs.* 2020 Nov 5:1-12. doi: 10.1007/s40265-020-01424-7. https://link.springer.com/article/10.1007/s40265-020-01424-7
Findings: The objectives of the study were to evaluate pharmacological treatment patterns by COVID-19 severity and identify the determinants of prescribing for COVID-19. Using electronic health record data from a large Massachusetts-based healthcare system, we identified all patients aged ≥ 18 years hospitalized with laboratory-confirmed COVID-19 from 1 March to 24 May, 2020. We defined five levels of COVID-19 severity at hospital admission: (1) hospitalized but not requiring supplemental oxygen; (2-4) hospitalized and requiring oxygen ≤ 2, 3-4, and ≥ 5 L per minute, respectively; and (5) intubated or admitted to an intensive care unit. We assessed the medications used to treat COVID-19 or as supportive care during hospitalization. Among 2821 patients hospitalized for COVID-19, we found inpatient mortality increased by severity from 5% for level 1 to 23% for level 5. As compared to patients with severity level 1, those with severity level 5 were 3.53 times more likely to receive a medication used to treat COVID-19. Other predictors of treatment were fever, low oxygen saturation, presence of co-morbidities, and elevated inflammatory biomarkers. The use of most COVID-19 relevant medications has dropped substantially while the use of remdesivir and therapeutic anticoagulants has increased over the study period. Careful consideration of disease severity and other determinants of COVID-19 drug use is necessary for appropriate conduct and interpretation of non-randomized studies evaluating outcomes of COVID-19 treatments.

31. **Prone positioning for patients intubated for severe acute respiratory distress syndrome (ARDS) secondary to COVID-19: a retrospective observational cohort study.** Weiss TT, Cerda F, Scott JB, et al. *Br J Anaesth.* 2020 Oct 10:S0007-0912(20)30837-0. doi: 10.1016/j.bja.2020.09.042. https://bjanaesthesia.org/article/S0007-0912(20)30837-0/abstract
Findings: Forty-two subjects (29 males; age: 52-69 yr) were eligible for analysis. Nine subjects were placed in the prone position only once, with 25 requiring prone positioning on three or more occasions. A total of 31/42 (74%) subjects survived to discharge, with five requiring ECMO; 11/42 (26%) subjects died. After the first prone positioning session, Pao2/Fio2 increased

from 17.9 kPa (7.2) to 28.2 kPa (12.2). After the initial prone positioning session, subjects who were discharged from hospital were more likely to have an improvement in Pao2/Fio2 ratio ≥20%, compared with those requiring ECMO or who died. Patients with COVID-19 acute respiratory distress syndrome frequently responded to initial prone positioning with improved oxygenation. Subsequent prone positioning in subjects discharged from hospital was associated with greater improvements in oxygenation.

32. **Significantly decreased mortality in a large cohort of COVID-19 patients transfused early with convalescent plasma containing high titer anti-SARS-CoV-2 spike protein IgG.** Salazar E, Christensen PA, Graviss EA, et al. *Am J Pathol.* 2020 Nov 3:S0002-9440(20)30489-2. doi: 10.1016/j.ajpath.2020.10.008. https://ajp.amjpathol.org/article/S0002-9440(20)30489-2/fulltext
    Findings: We recently reported results from interim analysis of a propensity-score matched study suggesting that early treatment of COVID-19 patients with convalescent plasma containing high titer anti-spike protein receptor binding domain (RBD) IgG significantly decreases mortality. We here present results from 60-day follow up of our cohort of 351 transfused hospitalized patients. Prospective determination of ELISA anti-RBD IgG titer facilitated selection and transfusion of the highest titer units available. Retrospective analysis by the Ortho VITROS IgG assay revealed a median signal/cutoff (S/C) ratio of 24.0 for transfused units, a value far exceeding the recently FDA-required cutoff of 12.0 for designation of high titer convalescent plasma. With respect to altering mortality, our analysis identified an optimal window of 44 hours post-hospitalization for transfusing COVID-19 patients with high titer convalescent plasma. In the aggregate, the analysis confirms and extends our previous preliminary finding that transfusion of COVID-19 patients soon after hospitalization with high titer anti-spike protein RBD IgG present in convalescent plasma significantly reduces mortality.

33. **Impact of late administration of corticosteroids in COVID-19 ARDS.** COVADIS study group investigators. *Intensive Care Med.* 2020 Nov 6. doi: 10.1007/s00134-020-06311-z. https://link.springer.com/article/10.1007/s00134-020-06311-z
    Findings: Early CTC treatment has demonstrated survival benefit in severe COVID-19 pneumonia, and has been endorsed by WHO. Conversely, no data are available on the impact of late CTC administration. This post hoc analysis of a homogeneous cohort of the most severe critically ill patients found that late CTC administration did not improve the patient-centered outcomes.

34. **Rescue therapy with inhaled nitric oxide and almitrine in COVID-19 patients with severe acute respiratory distress syndrome.** Bagate F, Tuffet S, Masi P, et al. *Ann Intensive Care.* 2020 Nov 4;10(1):151. doi: 10.1186/s13613-020-00769-2. https://annalsofintensivecare.springeropen.com/articles/10.1186/s13613-020-00769-2
    Findings: In COVID-19 patients with severe acute respiratory distress syndrome (ARDS), the relatively preserved respiratory system compliance despite severe hypoxemia, with specific pulmonary vascular dysfunction, suggests a possible hemodynamic mechanism for VA/Q mismatch, as hypoxic vasoconstriction alteration. This study aimed to evaluate the capacity of inhaled nitric oxide (iNO)-almitrine combination to restore oxygenation in severe C-ARDS

patients. Ten severe C-ARDS patients were assessed (7 males and 3 females), with a median age of 60 [52-72] years. Combination of iNO and almitrine outperformed iNO alone for oxygenation improvement. The median of PaO2/FiO2 ratio varied from 102 [89-134] mmHg at baseline, to 124 [108-146] mmHg after iNO ($p = 0.13$) and 180 [132-206] mmHg after iNO and almitrine ($p < 0.01$). We found no correlation between the increase in oxygenation caused by iNO-almitrine combination and that caused by proning. In this pilot study of severe C-ARDS patients, iNO-almitrine combination was associated with rapid and significant improvement of oxygenation. These findings highlight the role of pulmonary vascular function in COVID-19 pathophysiology.

35. **Effect of pre-exposure use of hydroxychloroquine on COVID-19 mortality: a population-based cohort study in patients with rheumatoid arthritis or systemic lupus erythematosus using the OpenSAFELY platform.** Rentsch CT, DeVito NJ, MacKenna B, et al. *The Lancet Rheumatology* Published: November 5, 2020. DOI: https://doi.org/10.1016/S2665-9913(20)30378-7
Findings: We found no evidence of a difference in COVID-19 mortality among people who received hydroxychloroquine for treatment of rheumatological disease before the COVID-19 outbreak in England. Therefore, completion of randomised trials investigating pre-exposure prophylactic use of hydroxychloroquine for prevention of severe outcomes from COVID-19 are warranted.

36. **Hydroxychloroquine vs. Azithromycin for Hospitalized Patients with COVID-19 (HAHPS): Results of a Randomized, Active Comparator Trial.** Brown SM, Peltan I, Kumar N, et al. *Ann Am Thorac Soc.* 2020 Nov 9. doi: 10.1513/AnnalsATS.202008-940OC.
https://www.atsjournals.org/toc/annalsats/0/ja
Findings: We enrolled 85 patients at 13 hospitals over 11 weeks. Adherence to study medication was high. The estimated odds ratio for less favorable status on the ordinal scale for hydroxychloroquine vs. azithromycin from the primary analysis was 1.07, with a 95% credible interval from 0.63 to 1.83 with a posterior probability of 60% that hydroxychloroquine was worse than azithryomycin. Secondary outcomes displayed a similar, slight preference for azithromycin over hydroxychloroquine. QTc prolongation was rare and did not differ between groups. The twenty safety outcomes were similar between arms with the possible exception of post-randomization onset acute kidney injury, which was more common with hydroxychloroquine (15% vs. 0%). Patients in the hydroxychloroquine arm received remdesivir more often than in the azithromycin arm (19% vs. 2%). There was no apparent association between remdesivir use and acute kidney injury. While early termination limits the precision of our results, we found no suggestion of substantial efficacy for hydroxychloroquine over azithromycin. Acute kidney injury may be more common with hydroxychloroquine than azithromycin, although this may be due to the play of chance. Differential use of remdesivir may have biased our results in favor of hydroxychloroquine. *Our results are consistent with conclusions from other trials that hydroxychloroquine cannot be recommended for inpatients with COVID-19; azithromycin may merit additional investigation.*

Transmission / Infection Control

37. **SARS-CoV-2 seroprevalence and transmission risk factors among high-risk close contacts: a retrospective cohort study.** Ng OT, Marimuthu K, Koh V, et al. *Lancet Infect Dis.* 2020 Nov 2:S1473-3099(20)30833-1. doi: 10.1016/S1473-3099(20)30833-1 https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30833-1/fulltext
Findings: Between Jan 23 and April 3, 2020, 7770 close contacts (1863 household contacts, 2319 work contacts, and 3588 social contacts) linked to 1114 PCR-confirmed index cases were identified. Symptom-based PCR testing detected 188 COVID-19 cases, and 7582 close contacts completed quarantine without a positive SARS-CoV-2 PCR test. Among 7518 (96·8%) of the 7770 close contacts with complete data, the secondary clinical attack rate was 5·9% for 1779 household contacts, 1·3% for 2231 work contacts, and 1·3% for 3508 social contacts. Sharing a bedroom and being spoken to by an index case for 30 min or longer were associated with SARS-CoV-2 transmission among household contacts. Among non-household contacts, exposure to more than one case, being spoken to by an index case for 30 min or longer, and sharing a vehicle with an index case were associated with SARS-CoV-2 transmission. Among both household and non-household contacts, indirect contact, meal sharing, and lavatory co-usage were not independently associated with SARS-CoV-2 transmission. Targeted community measures should include physical distancing and minimising verbal interactions. Testing of all household contacts, including asymptomatic individuals, is warranted.

38. **Survival of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and Influenza Virus on Human Skin: Importance of Hand Hygiene in Coronavirus Disease 2019 (COVID-19).** Hirose R, Ikegaya H, Naito Y, et al. *Clinical Infectious Diseases*, 03 October 2020. https://doi.org/10.1093/cid/ciaa1517
Findings: There is a 9-hour survival of SARS-CoV-2 on human skin. Proper hand hygiene is important to prevent the spread of SARS-CoV-2 infections.

39. **Unintended consequences of infection prevention and control measures during COVID-19 pandemic.** Wee LE, Conceicao EP, Tan JY, et al. *Am J Infect Control.* 2020 Nov 3:S0196-6553(20)30963-9. doi: 10.1016/j.ajic.2020.10.019. https://www.ajicjournal.org/article/S0196-6553(20)30963-9/abstract
Findings: Enhanced IPC measures introduced to contain COVID-19 had the unintended positive consequence of containing HA-RVI. The cumulative incidence of HA-RVI decreased from 9.69 cases per 10,000 patient-days to 0.83 cases per 10,000 patient-days. Hospital-wide MRSA acquisition rates declined significantly during the pandemic, together with central-line-associated-bloodstream infection (CLABSI) rates; likely due to increased compliance with Standard Precautions. Despite the disruption caused by the pandemic, there was no increase in CP-CRE acquisition, and rates of other HAIs remained stable. Multimodal IPC strategies can be implemented at scale to successfully mitigate healthcare-associated transmission of RVIs. Good adherence to personal-protective-equipment and hand hygiene kept other HAI rates stable even during an ongoing pandemic where respiratory infections were prioritized for interventions.

40. **Aerosol persistence in relation to possible transmission of SARS-CoV-2.** Smith SH, Somsen GA, van Rijn C, et al. *Phys Fluids*. 2020 Oct 1;32(10):107108. https://aip.scitation.org/doi/10.1063/5.0027844
Findings: By measuring and modeling the dynamics of exhaled respiratory droplets, we can assess the relative contribution of aerosols to the spreading of SARS-CoV-2. We measure size distribution, total numbers, and volumes of respiratory droplets, including aerosols, by speaking and coughing from healthy subjects. Dynamic modeling of exhaled respiratory droplets allows us to account for aerosol persistence times in confined public spaces. The probability of infection by inhalation of aerosols when breathing in the same space can then be estimated using current estimates of viral load and infectivity of SARS-CoV-2. The current known reproduction numbers show a lower infectivity of SARS-CoV-2 compared to, for instance, measles, which is known to be efficiently transmitted through the air. In line with this, our study of transmission of SARS-CoV-2 suggests that aerosol transmission is a possible but perhaps not a very efficient route, in particular from non-symptomatic or mildly symptomatic individuals that exhibit low viral loads.

41. **Association between Nursing Home Crowding and COVID-19 Infection and Mortality in Ontario, Canada.** Brown KA, Jones A, Daneman N, et al. *JAMA Intern Med.* 2020 Nov 9. doi: 10.1001/jamainternmed.2020.6466.
https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/10.1001/jamainternmed.2020.6466
Findings: Of 623 homes in Ontario, we obtained complete information on 618 homes (99%) housing 78607 residents (women, 54 160 [68.9%]; age ≥85 years, 42 919 [54.6%]). A total of 5218 residents (6.6%) developed COVID-19 infection, and 1452 (1.8%) died of COVID-19 infection as of May 20, 2020. COVID-19 infection was distributed unevenly across nursing homes; 4496 infections (86%) occurred in 63 homes (10%). Simulations suggested that converting all 4-bed rooms to 2-bed rooms would have averted 998 COVID-19 cases (19.1%) and 263 deaths (18.1%). In this cohort of Canadian nursing homes, crowding was common and crowded homes were more likely to experience larger and deadlier COVID-19 outbreaks.

Vaccine

42. **Randomized, double-blinded and placebo-controlled phase II trial of an inactivated SARS-CoV-2 vaccine in healthy adults.** Che Y, Liu X, Pu Y, et al. *Clin Infect Dis.* 2020 Nov 9:ciaa1703. doi: 10.1093/cid/ciaa1703. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1703/5962856
Findings: In this randomized, double-blinded and controlled trial, healthy adults received a medium (MD) or a high dose (HD) of the vaccine at an interval of either 14 days or 28 days. Neutralizing antibody (NAb) and anti-S and anti-N antibodies were detected at different times, and adverse reactions were monitored for 28 days after full immunization. A total of 742 adults were enrolled in the immunogenicity and safety analysis. Among subjects in the 0, 14 procedure, the seroconversion rates of NAb in MD and HD groups were 89% and 96% with GMTs of 23 and 30, respectively, at day 14 and 92% and 96% with GMTs of 19 and 21, respectively at day 28 after immunization. Anti-S antibodies had GMTs of 1883 and 2370 in MD

and 2295 and 2432 in HD group. Anti-N antibodies had GMTs of 387 and 434 in MD group and 342 and 380 in HD group. Among subjects in the 0, 28 procedure, seroconversion rates for NAb at both doses were both 95% with GMTs of 19 at day 28 after immunization. Anti-S antibodies had GMTs of 937 and 929 for MD and HD group, and anti-N antibodies had GMTs of 570 and 494 for MD and HD group, respectively. No serious adverse events were observed during the study period. Adults vaccinated with inactivated SARS-CoV-2 vaccine had NAb as well as anti-S/N antibody and had a low rate of adverse reactions.

***See Pfizer press release below**

Women & Children

43. **Extremely Premature Infants, Scarcity, and the COVID-19 Pandemic.** Kaempf JW, Dirksen KM, Kockler NJ. **[PSJH authors]**. *Acta Paediatr.* 2020 Nov 3. doi: 10.1111/apa.15651. https://onlinelibrary.wiley.com/doi/abs/10.1111/apa.15651
Scarcity is Nature's creative provenance, the wellspring of human conflict and subsequent adaptation. Deficiencies of food, shelter, and basic safety are primary, but secondary privations real or imagined (material comforts, money, power, sex), are often perceived insufficient by humankind and drive history's discord. The COVID-19 pandemic spotlights scarcity and resource allocation, and we hope rational scrutiny of value in healthcare (benefits accrued/resources consumed). Physicians are more aware of this historic opportunity to thoughtfully study value considerations as objective metrics that can facilitate reasoned analysis, innovation, and justice.

44. **Distinct antibody responses to SARS-CoV-2 in children and adults across the COVID-19 clinical spectrum,** Weisberg SP, Connors TJ, Farber DL. *Nature Immunology* (2020). https://www.nature.com/articles/s41590-020-00826-9
Findings: Here, we show distinct antibody responses in children and adults after SARS-CoV-2 infection. Adult COVID-19 cohorts had anti-spike (S) IgG, IgM and IgA antibodies, as well as anti-nucleocapsid (N) IgG antibody, while children with and without MIS-C had reduced breadth of anti-SARS-CoV-2-specific antibodies, predominantly generating IgG antibodies specific for the S protein but not the N protein. Moreover, children with and without MIS-C had reduced neutralizing activity as compared to both adult COVID-19 cohorts, indicating a reduced protective serological response. These results suggest a distinct infection course and immune response in children independent of whether they develop MIS-C, with implications for developing age-targeted strategies for testing and protecting the population.

45. **Characteristics and outcomes of neonatal SARS-CoV-2 infection in the UK: a prospective national cohort study using active surveillance.** Gale C, Quigley MA, Placzek A, et al. *The Lancet Child & Adolescent Health* Published: November 9, 2020 DOI: https://doi.org/10.1016/S2352-4642(20)30342-4
Findings: We identified 66 babies with confirmed SARS-CoV-2 infection (incidence 5·6 per 10 000 livebirths), of whom 28 (42%) had severe neonatal SARS-CoV-2 infection (incidence 2·4 [1·6–3·4] per 10 000 livebirths). 16 (24%) of these babies were born preterm. 36 (55%) babies were from white ethnic groups (SARS-CoV-2 infection incidence 4·6 per 10 000 livebirths), 14

(21%) were from Asian ethnic groups (15·2 [8·3–25·5] per 10 000 livebirths), eight (12%) were from Black ethnic groups (18·0 [7·8–35·5] per 10 000 livebirths), and seven (11%) were from mixed or other ethnic groups (5·6 [2·2–11·5] per 10 000 livebirths). 17 (26%) babies with confirmed infection were born to mothers with known perinatal SARS-CoV-2 infection, two (3%) were considered to have possible vertically acquired infection (SARS-CoV-2-positive sample within 12 h of birth where the mother was also positive). Eight (12%) babies had suspected nosocomially acquired infection. As of July 28, 2020, 58 (88%) babies had been discharged home, seven (11%) were still admitted, and one (2%) had died of a cause unrelated to SARS-CoV-2 infection. Neonatal SARS-CoV-2 infection is uncommon in babies admitted to hospital. Infection with neonatal admission following birth to a mother with perinatal SARS-CoV-2 infection was unlikely, and possible vertical transmission rare, supporting international guidance to avoid separation of mother and baby. The high proportion of babies from Black, Asian, or minority ethnic groups requires investigation.

46. **Acute Cardiovascular Manifestations in 286 Children with Multisystem Inflammatory Syndrome Associated with COVID-19 Infection in Europe.** Valverde I, Singh Y, Sanchez-de-Toledo J, et al. *Circulation.* 2020 Nov 9. doi: 10.1161/CIRCULATIONAHA.120.050065. https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.050065
Findings: A total of 286 children from 55 centers in 17 European countries were included. The median age was 8.4 years and 67% were males. The most common cardiovascular complications were shock, cardiac arrhythmias, pericardial effusion and coronary artery dilatation. Reduced left ventricular ejection fraction was present in over half of the patients and a vast majority of children had raised cardiac troponin (cTnT) when checked. The biochemical markers of inflammation were raised in majority of patients on admission: elevated CRP, serum ferritin, procalcitonin, NT-proBNP, IL-6 level and D-dimers. There was a statistically significant correlation between degree of elevation in cardiac and biochemical parameters and need for intensive care support ($p < 0.05$). Polymerase chain reaction (PCR) for SARS-CoV-2 was positive in 33.6% while IgM and IgG antibodies were positive in 15.7% and IgG 43.6 % cases, respectively when checked. One child died in the study cohort. Cardiac involvement is common in children with multisystem inflammatory syndrome associated with Covid-19 pandemic. A majority of children have significantly raised levels of NT pro-BNP, ferritin, D-dimers and cardiac troponin in addition to high CRP and procalcitonin levels. Compared to adults with Covid-19, mortality in children with MIS-C is uncommon despite multi-system involvement, very elevated inflammatory markers and need for intensive care support.

47. **Public health antibody screening indicates a six-fold higher SARS-CoV-2 exposure rate than reported cases in children.** Hippich M, Holthaus L, Assfalg R, et al. *Med (N Y)*. 2020 Oct 29. doi: 10.1016/j.medj.2020.10.003.
https://www.sciencedirect.com/science/article/pii/S2666634020300209
Findings: We developed a highly specific and sensitive approach to measuring antibodies against SARS-CoV-2 for population-scale immune surveillance. Antibody positivity was defined as a dual-positive response against both the receptor binding domain and nucleocapsid proteins of SARS-CoV-2. Antibodies were measured by immuno-precipitation assays in capillary blood from 15,771 children aged 1 to 18 years living in Bavaria, Germany, and participating in a

public health type 1 diabetes screening program, in 1,916 dried blood spots from neonates in a Bavarian screening study, and in 75 SARS-CoV-2 positive individuals. Dual-antibody positivity was detected in none of 3887 children in 2019 (100% specificity) and 73 of 75 SARS-CoV-2 positive individuals (97.3% sensitivity). Antibody surveillance in children during 2020 resulted in frequencies of 0.08% in January to March, 0.61% in April, 0.74% in May, 1.13% in June and 0.91% in July. Antibody prevalence from April 2020 was six-fold higher than the incidence of authority-reported cases (156 per 100,000 children), showed marked variation between the seven Bavarian regions (P<0.0001), and was not associated with age or sex. Transmission in children with virus-positive family members was 35%; 47% of positive children were asymptomatic. No association with type 1 diabetes autoimmunity was observed. Antibody frequency in newborns was 0.47%. We demonstrate the value of population-based screening programs for pandemic monitoring.

GUIDELINES & CONSENSUS STATEMENTS

American College of Rheumatology Guidance for the Management of Rheumatic Disease in Adult Patients During the COVID-19 Pandemic: Use of Apremilast. *Arthritis Rheumatol.* 2020 Nov 3. doi: 10.1002/art.41575.

Summary of International Recommendations for Donation and Transplantation Programs During the Coronavirus Disease (COVID-19) Pandemic. *Transplantation*. 2020 Oct 30. doi: 10.1097/TP.0000000000003520.

A consensus statement for the management and rehabilitation of communication and swallowing function in the ICU: A global response to COVID-19. COVID-19 SLP Global Group. *Arch Phys Med Rehabil.* 2020 Nov 6:S0003-9993(20)31210-7. doi: 10.1016/j.apmr.2020.10.113.

FDA / CDC / NIH / WHO Updates

CDC - Interim U.S. Guidance for Risk Assessment and Work Restrictions for Healthcare Personnel with Potential Exposure to COVID-19, Nov 5 2020.

FDA - Authorizes Monoclonal Antibody for Treatment of COVID-19, Nov 9 2020.

NIH - Hydroxychloroquine does not benefit adults hospitalized with COVID-19, Nov 9 2020. *see JAMA article under Therapeutics

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Press Release / Commentary

PFIZER AND BIONTECH ANNOUNCE VACCINE CANDIDATE AGAINST COVID-19 ACHIEVED SUCCESS IN FIRST INTERIM ANALYSIS FROM PHASE 3 STUDY, Nov 9, 2020.

Institutional versus home isolation to curb the COVID-19 outbreak. *Lancet*. 2020 Nov 6:S0140-6736(20)32161-9. doi: 10.1016/S0140-6736(20)32161-9.

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