

### **COVID-19 Resource Desk**

#17 | 8.12.2020 to 8.18.2020

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

\*not a retraction, but follow-up to a previous article - **Role of children in household transmission of COVID-19.** Kim J, Choe YJ, Lee J, et al. *Archives of Disease in Childhood*. 07 August 2020. doi: 10.1136/archdischild-2020-319910

https://adc.bmj.com/content/early/2020/08/06/archdischild-2020-319910

Findings: A study by researchers in South Korea last month suggested that children between the ages of 10 and 19 spread the coronavirus more frequently than adults — a widely reported finding that influenced the debate about the risks of reopening schools. But additional data from the research team now calls that conclusion into question; it's not clear who was infecting whom. Some of the household members who appeared in the initial report to have been infected by older children in fact were exposed to the virus at the same time as the children. All of them may have been infected by contacts they shared. The disclosure does not negate the overall message of that study, experts said: Children under age 10 do not spread the virus as much as adults do, and the ability to transmit seems to increase with age.

\*See previous article - **Contact tracing during coronavirus disease outbreak, South Korea, 2020.** Park YJ, Choe YJ, Park O, et al. *Emerg Infect Dis.* 2020 Oct. https://doi.org/10.3201/eid2610.201315. Original Publication Date: July 16, 2020

**Basic Science / Virology / Pre-clinical** 

1. Crippling life support for SARS-CoV-2 and other viruses through synthetic lethality. Mast FD, Navare AT, Almer M van der Sloot [*PSJH authors*]. *J Cell Biol*. 2020 Oct 5;219(10):e202006159. doi: 10.1083/jcb.202006159.

https://rupress.org/jcb/article/219/10/e202006159/152015/Crippling-life-support-for-SARS-CoV-2-and-other

Findings: With the rapid global spread of SARS-CoV-2, we have become acutely aware of the inadequacies of our ability to respond to viral epidemics. Although disrupting the viral life cycle is critical for limiting viral spread and disease, it has proven challenging to develop targeted and selective therapeutics. Synthetic lethality offers a promising but largely unexploited strategy against infectious viral disease; as viruses infect cells, they abnormally alter the cell state, unwittingly exposing new vulnerabilities in the infected cell. Therefore, we propose that effective therapies can be developed to selectively target the virally reconfigured host cell

networks that accompany altered cellular states to cripple the host cell that has been converted into a virus factory, thus disrupting the viral life cycle.

#### **Clinical Syndrome**

2. Acute SARS-CoV-2 Infection Impairs Dendritic Cell and T Cell Responses. Zhou R, To KK, Wong YC, et al. *Immunity*. 2020 Aug 4:S1074-7613(20)30333-2. doi: 10.1016/j.immuni.2020.07.026. https://tinyurl.com/yyu6j6uk

Findings: The SARS-CoV-2 pandemic has resulted in millions of infections, yet the role of host immune responses in early COVID-19 pathogenesis remains unclear. By investigating 17 acute and 24 convalescent patients, we found that acute SARS-CoV-2 infection resulted in broad immune cell reduction including T, natural killer, monocyte, and dendritic cells (DCs). DCs were significantly reduced with functional impairment, and ratios of conventional DCs to plasmacytoid DCs were increased among acute severe patients. Besides lymphocytopenia, although neutralizing antibodies were rapidly and abundantly generated in patients, there were delayed receptor binding domain (RBD)- and nucleocapsid protein (NP)-specific T cell responses during the first 3 weeks after symptoms onset. Moreover, acute RBD- and NP-specific T cell responses included relatively more CD4 T cells than CD8 T cells. Our findings provided evidence that impaired DCs, together with timely inverted strong antibody but weak CD8 T cell responses, could contribute to acute COVID-19 pathogenesis and have implications for vaccine development.

#### **Diagnostics & Screening**

3. Comparison analysis of different swabs and transport mediums suitable for SARS-CoV-2 testing following shortages. Garnett L, Bello A, Tran KN, et al. *J Virol Methods.* 2020 Aug 8:113947. doi: 10.1016/j.jviromet.2020.113947.

#### https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7414358/

Findings: The high demand for testing has resulted in a depletion of recommended swabs and viral transport media required for nasopharyngeal sampling. Therefore, the potential use of unvalidated alternatives must be explored to address the global shortage of testing supplies. To tackle this issue, we evaluated the utility of different swabs and transport mediums for the molecular detection of SARS-CoV-2. This study compared the performance of six swabs commonly found in primary and tertiary health care settings (PurFlock Ultra, FLOQSwab, Puritan Pur-Wraps cotton tipped applicators, Puritan polyester tipped applicators, MedPro 6" cotton tipped applicators, and HOLOGIC Aptima) for their efficacy in testing for SARS-CoV-2. Separately, the molecular detection of SARS-CoV-2 was completed from different transport mediums (DMEM, PBS, 100 % ethanol, 0.9 % normal saline and VTM), which were kept up to three days at room temperature (RT). The results indicate that there is no meaningful difference in viral yield from different swabs and most transport mediums for the collection and detection of SARS-CoV-2, indicating swab and medium alternatives could be used if supplies run out.

4. **A SARS-CoV-2 Prediction Model from Standard Laboratory Tests.** Bayat V, Phelps S, Ryono R, et al. *Clin Infect Dis.* 2020 Aug 12:ciaa1175. doi: 10.1093/cid/ciaa1175.

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1175/5891814 Findings: In a cohort of 75,991 veteran inpatients and outpatients who tested for SARS-CoV-2 in the months of March through July, 2020, 7,335 of whom were positive by RT-PCR or antigen testing, and who had at least 15 of 20 lab results within the window period, our model predicted the results of the SARS-CoV-2 test with a specificity of 86.8%, a sensitivity of 82.4%, and an overall accuracy of 86.4%. While molecular-based and antibody tests remain the reference standard method for confirming a SARS-CoV-2 diagnosis, their clinical sensitivity is not well known. The model described herein may provide a complementary method of determining SARS-CoV-2 infection status, based on a fully independent set of indicators, that can help confirm results from other tests as well as identify positive cases missed by molecular testing.

 Facility-Wide Testing for SARS-CoV-2 in Nursing Homes - Seven U.S. Jurisdictions, March-June 2020. Hatfield KM, Reddy SC, Forsberg K, et al. MMWR Morb Mortal Wkly Rep. 2020 Aug 11;69(32):1095-1099. doi: 10.15585/mmwr.mm6932e5.

https://www.cdc.gov/mmwr/volumes/69/wr/mm6932e5.htm

Findings: Seven state or local health departments conducted initial facility-wide testing of residents and staff members in 288 nursing homes during March 24-June 14, 2020. Two of the seven health departments conducted testing in 195 nursing homes as part of facility-wide testing all nursing homes in their state, which were in low-incidence areas; 125 of the 195 nursing homes had not reported any COVID-19 cases before the testing. Ninety-five of 22,977 (0.4%) persons tested in 29 (23%) of these 125 facilities had positive SARS-CoV-2 test results. The other five health departments targeted facility-wide testing to 93 nursing homes, where 13,443 persons were tested, and 1,619 (12%) had positive SARS-CoV-2 test results. In regression analyses among 88 of these nursing homes with a documented case before facility-wide testing occurred, each additional day between identification of the first case and completion of facilitywide testing was associated with identification of 1.3 additional cases. Among 62 facilities that could differentiate results by resident and HCP status, an estimated 1.3 HCP cases were identified for every three resident cases. Performing facility-wide testing immediately after identification of a case commonly identifies additional unrecognized cases and, therefore, might maximize the benefits of infection prevention and control interventions. In contrast, facility-wide testing in low-incidence areas without a case has a lower proportion of test positivity; strategies are needed to further optimize testing in these settings.

 SARS-CoV-2 PCR testing of skin for COVID-19 diagnostics: a case report. Jamiolkowski D, Mühleisen B, Müller S, et al. *Lancet*. August 13, 2020 DOI:https://doi.org/10.1016/S0140-6736(20)31754-2

https://www.sciencedirect.com/science/article/pii/S0140673620317542?via%3Dihub Findings: We report the case of an 81-year-old woman who presented with a temperature of up to 39°C and a generalised macular eruption with partial vasculitis-like patterns and palmoplantar accentuation. Infection with SARS-CoV-2 was suspected but a SARS-CoV-2 PCR (nasopharyngeal swab, Cobas SARS-CoV-2 Test, Roche Diagnostics, Rotkreuz, Switzerland) was negative. 2 days later, a lesional whole skin 4 mm punch biopsy sample was taken from the left flank. Over the next 2 weeks, the patient's rash gradually improved. 6 weeks later, serology tests against anti-SARS-CoV-2 antibodies (Elecsys Anti-SARS-CoV-2, Roche Diagnostics, Rotkreuz, Switzerland) were negative. However, PCR testing of the skin using established methods1 detected SARS-CoV-2 at low copy numbers (37 per 1 × 106 human RPPH1 copies). This case is important because it highlights the shortcomings of currently available testing methods for SARS-CoV-2 infection. Although the sensitivity and specificity of currently available PCR and serology tests are high, swab samples that are taken incorrectly are known drivers of the relatively large number of false negative tests for SARS-CoV-2. This case emphasises the use of SARS-CoV-2 PCR testing of skin biopsy samples as an additional diagnostic tool.

#### **Epidemiology & Public Health**

- 7. Burden of illness in households with SARS-CoV-2 infected children. Teherani MF, Kao CM, Camacho-Gonzalez A, et al. J Pediatric Infect Dis Soc. 2020 Aug 11:piaa097. doi: 10.1093/jpids/piaa097. https://academic.oup.com/jpids/advance-article/doi/10.1093/jpids/piaa097/5891283?searchresult=1
  Findings: We investigated the dynamics of illness among household members of SARS-CoV-2 infected children that received medical care (n=32). We identified 144 household contacts (HCs): 58 children and 86 adults. Forty-six percent of HCs developed symptoms consistent with COVID-19 disease. Child-to-adult transmission was suspected in 7 cases.
- Mental Health, Substance Use, and Suicidal Ideation During the COVID-19 Pandemic United States, June 24–30, 2020. Czeisler MÉ, Lane RI, Petrosky E, et al. MMWR Morb Mortal Wkly Rep 2020;69:1049–1057. DOI: <u>http://dx.doi.org/10.15585/mmwr.mm6932a1</u> <u>https://www.cdc.gov/mmwr/volumes/69/wr/mm6932a1.htm</u>

Findings: During June 24–30, 2020, U.S. adults reported considerably elevated adverse mental health conditions associated with COVID-19. Younger adults, racial/ethnic minorities, essential workers, and unpaid adult caregivers reported having experienced disproportionately worse mental health outcomes, increased substance use, and elevated suicidal ideation.

9. Comparison of Estimated Excess Deaths in New York City During the COVID-19 and 1918 Influenza Pandemics. Faust JS, Lin Z, del Rio C. *JAMA Netw Open.* 2020;3(8):e2017527. doi:10.1001/jamanetworkopen.2020.17527

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2769236

Findings: During the 1918 H1N1 influenza pandemic, there were approximately 50 million influenza-related deaths worldwide, including 675,000 in the US. This cohort study found that the absolute increase in deaths over baseline (ie, excess mortality) observed during the peak of 1918 H1N1 influenza pandemic was higher than but comparable to that observed during the first 2 months of the COVID-19 outbreak in New York City. However, because baseline mortality rates from 2017 to 2019 were less than half that observed from 1914 to 1917 owing to improvements in hygiene and modern achievements in medicine, public health, and safety, the relative increase during early COVID-19 period was substantially greater than during the peak of the 1918 H1N1 influenza pandemic.

- 10. Contact Settings and Risk for Transmission in 3410 Close Contacts of Patients With COVID-19 in Guangzhou, China: A Prospective Cohort Study. Luo L, Liu D, Liao X, et al. *Ann Intern Med*. 2020 Aug 13. doi: 10.7326/M20-2671.<u>https://www.acpjournals.org/doi/10.7326/M20-2671</u> Findings: Among 3,410 close contacts, 127 (3.7%) were secondarily infected. Of these 127 persons, 8 (6.3%) were asymptomatic. Of the 119 symptomatic cases, 20 (16.8%) were defined as mild, 87 (73.1%) as moderate, and 12 (10.1%) as severe or critical. Compared with the household setting (10.3%), the secondary attack rate was lower for exposures in healthcare settings (1.0%; odds ratio [OR], 0.09 [CI, 0.04 to 0.20]) and on public transportation (0.1%; OR, 0.01 [CI, 0.00 to 0.08]). The secondary attack rate increased with the severity of index cases, from 0.3% (CI, 0.0 to 1.0%) for asymptomatic to 3.3% (CI, 1.8% to 4.8%) for mild, 5.6% (CI, 4.4% to 6.8%) for moderate, and 6.2% (CI, 3.2% to 9.1%) for severe or critical cases. Index cases with expectoration were associated with higher risk for secondary infection (13.6% vs. 3.0% for index cases without expectoration; OR, 4.81 [CI, 3.35 to 6.93]). Household contact was the main setting for transmission of SARS-CoV-2, and the risk for transmission of SARS-CoV-2 among close contacts increased with the severity of index cases.
- 11. Characteristics and Outcomes of COVID-19 Patients During Initial Peak and Resurgence in the Houston Metropolitan Area. Vahidy FS, Drews AL, Masud FN, et al. *JAMA*. 2020 Aug 13. doi: 10.1001/jama.2020.15301. https://jamanetwork.com/journals/jama/fullarticle/2769610 Findings: As of July 7, 2020, 2,904 unique COVID-19 patients had been hospitalized, representing 774 and 2,130 patients during surge 1 and 2, respectively. Surge 2 data indicated a demographic shift of the pandemic toward a younger, predominantly Hispanic, and lower socioeconomic patient population with an overall lower comorbidity burden, ICU admission rate, and in-hospital mortality. Additionally, in-hospital mortality among ICU-treated surge 2 patients was 4.6% lower than that in surge 1. The overall better outcomes during surge 2 may be explained by a combination of lower comorbidity burden, lesser disease severity, and better medical management.
- 12. Periodic Oscillations in Daily Reported Infections and Deaths for Coronavirus Disease 2019. Bukhari Q, Jameel Y, Massaro JM, et al. *JAMA Netw Open*. 2020;3(8):e2017521. August 17, 2020. doi:10.1001/jamanetworkopen.2020.17521

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2769312

Findings: The trend of COVID-19 cases is not similar across countries, with several countries experiencing a decrease in the daily reported cases and deaths, while several others are reporting a surge in the daily reported cases and deaths. Studies of prior epidemics have suggested oscillatory patterns and cyclicity when analyzing long-term (ie, decades) epidemiological data. However, to our knowledge, high-frequency oscillations (ie, weekly) have not been reported during prior epidemics. We identified oscillatory patterns in the daily reported new cases and deaths with a periodicity of approximately 1 week for the US, Germany, Canada, Italy, Brazil, and the United Kingdom. It is possible that these periodic oscillations in daily reported cases are associated with testing bias, with higher rates of testing during certain days of a week. However, these periodic oscillations were also observed for positive test rates, suggesting that other variables, such as epidemiological or social factors

leading to higher transmission on certain days, might be associated with these oscillations. These oscillations should be included in the estimation of the effective reproduction number (Rt), similar to the way seasonality is accounted for in influenza. We urge the scientific community to conduct an in-depth exploration of the periodicity in COVID-19 cases and deaths, which might lead to improved COVID-19 predictions and understanding of the transmission of the disease.

13. Assessment of COVID-19 Hospitalizations by Race/Ethnicity in 12 States. Karaca-Mandic P, Georgiou A, Sen S. JAMA Intern Med. 2020 Aug 17. doi: 10.1001/jamainternmed.2020.3857. <u>https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2769369</u> Findings: This analysis identified considerable disparities in the prevalence of COVID-19 across racial/ethnic subgroups of the population in 12 US states. These findings are consistent with earlier studies. These findings highlight the need for increased data reporting and consistency within and across all states. Only 12 of 50 US states have consistently reported hospitalizations by race/ethnicity during our study period. The present study is limited in that there was no adjustment for age, sex, comorbidities, and socioeconomic factors within each racial/ethnic group that are likely to be associated with COVID-19 hospitalizations.

#### Healthcare Delivery & Healthcare Workers

 A California Hospital's Response to COVID-19: From a Ripple to a Tsunami Warning. Mary Kay Bader, Annabelle Braun, Cherie Fox, Lauren Dwinell, Jennifer Cord, Marne Andersen, Bryan Noakes, Daniel Ponticiello [*PSJH authors*]. Crit Care Nurse. 2020 Aug 17; e1-e16. doi: 10.4037/ccn2020799.

https://aacnjournals.org/ccnonline/article/doi/10.4037/ccn2020799/31134/A-California-Hospital-s-Response-to-COVID-19-From

Findings: An evidence-based question was developed and an extensive review of the literature was completed, resulting in a structured plan for the intensive care units to manage a surge of patients critically ill with COVID-19 in March 2020. Using a framework based on the literature reviewed, the Critical Care Services task force controlled the surge of patients with COVID-19 in March through May 2020. Patients received excellent care, and the mortality rate was 0.008%. The intensive care unit team had the needed respiratory and general supplies but had to continually adapt to shortages of personal protective equipment, cleaning products, and some medications. The intensive care unit pandemic response plan has been established and the team is prepared for the next wave of COVID-19.

15. Association of Nursing Home Ratings on Health Inspections, Quality of Care, and Nurse Staffing With COVID-19 Cases. Figueroa JF, Wadhera RK, Papanicolas I, et al. *JAMA*. 2020 Aug 10. doi: 10.1001/jama.2020.14709.

https://jamanetwork.com/journals/jama/fullarticle/2769437

Findings: Across 8 states, high-performing NHs for nurse staffing had fewer COVID-19 cases than low-performing NHs. In contrast, there was no significant difference in the burden of COVID-19 cases between high- vs low-performing NHs for health inspection or quality measure ratings. These findings suggest that poorly resourced NHs with nurse staffing shortages may be more susceptible to the spread of COVID-19. Although guidance on best practices on infection control are important, which has been the primary strategy used by CMS to date, policies that provide immediate staffing support may be more effective at mitigating the spread of COVID-19.

16. Coronavirus Disease 2019 Outcomes in French Nursing Homes That Implemented Staff Confinement with Residents. Belmin J, Um-Din N, Donadio C, et al. *JAMA Netw Open*. 2020 Aug 3;3(8):e2017533. doi:10.1001/jamanetworkopen.2020.17533.

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2769241

Findings: This study included 17 nursing homes in which 794 staff members confined themselves to the facility with their 1,250 residents. Only 1 nursing home with staff who self-confined (5.8%) had cases of COVID-19 among residents, compared with 4,599 facilities in the national survey (48.3%). Five residents (0.4%) in the nursing homes with staff who self-confined had confirmed COVID-19, compared with 30,569 residents (4.4%) with confirmed COVID-19 in the national survey. Five residents (0.4%) in the nursing homes with staff who self-confined died of COVID-19, compared with 12,516 (1.8%) in the national survey. These findings suggest that self-confinement of staff members with residents may help protect nursing home residents from mortality related to COVID-19 and residents and staff from COVID-19 infection.

17. Coronavirus 2019 (COVID-19) Infections Among Healthcare Workers, Los Angeles County, February - May 2020. Hartmann S, Rubin Z, Sato H, et al. *Clin Infect Dis*. 2020 Aug 17;ciaa1200. doi: 10.1093/cid/ciaa1200.

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1200/5893141

Findings: As of May 31st, over three months into the pandemic, nearly 5,500 positive HCWs were reported to LAC DPH, representing 9.6% of all cases. Cases reported working in 27 different setting types, including outpatient medical offices, correctional facilities, emergency medical services, etc., with the highest proportion from long-term care facilities (46.6%) and hospitals (27.7%). Case-patients included both clinical and non-clinical roles, with nearly half (49.4%) of positive HCWs being nurses. Over two-thirds of HCWs (68.6%) worked at some point during their infectious period and nearly half (47.9%) reported a known exposure to a positive patient and/or co-worker within their facility. Overall, compared to all LAC cases, HCWs reported lower rates of hospitalization (5.3% vs. 12.2%) and death (0.7% vs. 4.3%) from COVID-19.

#### **Laboratory Results**

18. **Regulatory T Cells Tested in Patients With COVID-19 ARDS.** Abbasi J. *JAMA*. 2020 Aug 11;324(6):539. doi: 10.1001/jama.2020.13765.

https://jamanetwork.com/journals/jama/fullarticle/2769243

Findings: Two men with coronavirus disease 2019 (COVID-19) acute respiratory distress syndrome (ARDS) survived after treatment with off-the-shelf regulatory T cells, also known as Tregs, Johns Hopkins physicians recently reported. The investigational allogenic Tregs with lung-homing markers were derived from cord blood.

## 19. Systems biological assessment of immunity to mild versus severe COVID-19 infection in humans. Arunachalam PS, Wimmers F, Mok CKP, et al. *Science*. 2020 Aug 11:eabc6261. doi: 10.1126/science.abc6261.

https://science.sciencemag.org/content/early/2020/08/10/science.abc6261

Findings: We analyzed immune responses in 76 COVID-19 patients and 69 healthy individuals from Hong Kong and Atlanta. In PBMCs of COVID-19 patients, there was reduced expression of HLA-DR and pro-inflammatory cytokines by myeloid cells, and impaired mTOR-signaling and IFN- $\alpha$  production by plasmacytoid DCs. In contrast, there were enhanced plasma levels of inflammatory mediators, including EN-RAGE, TNFSF14, and oncostatin-M, which correlated with disease severity and increased bacterial products in human plasma. Single-cell transcriptomics revealed no type-I IFN, reduced HLA-DR in myeloid cells of severe patients, and transient expression of IFN-stimulated genes. This was consistent with bulk PBMC transcriptomics, and transient, low plasma IFN- $\alpha$  levels during infection. These results reveal mechanisms and potential therapeutic targets for COVID-19.

#### Prognosis

20. Impact of cardiovascular risk profile on COVID-19 outcome. A meta-analysis. Sabatino J, De Rosa S, Di Salvo G, Indolfi C. *PLOS One.* 2020 Aug 14. doi:

https://doi.org/10.1371/journal.pone.0237131

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0237131

Findings: Among 77,317 hospitalized patients from 21 studies, 12.86% had cardiovascular comorbidities or RF. Cardiovascular complications were registered in 14.09% of cases during hospitalization. At meta-regression analysis, pre-existing cardiovascular comorbidities or RF were significantly associated to cardiovascular complications in COVID-19 patients (p = 0.019). Pre-existing cardiovascular comorbidities or RF (p<0.001), older age (p<0.001), and the development of cardiovascular complications during the hospitalization (p = 0.038) had a significant interaction with death. Cardiovascular complications are frequent among COVID-19 patients, and might contribute to adverse clinical events and mortality, together with pre-existing cardiovascular comorbidities and RF. Clinicians worldwide should be aware of this association, to identifying patients at higher risk.

21. Development and validation of a prediction model for severe respiratory failure in hospitalized patients with SARS-Cov-2 infection: a multicenter cohort study (PREDI-CO study). Bartoletti M, Giannella M, Scudeller L, et al. *Clin Microbiol Infect*. 2020 Aug 8:S1198-

743X(20)30479-1. doi: 10.1016/j.cmi.2020.08.003.

<u>https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30479-1/fulltext</u> Findings: We analyzed 1,113 patients (644 derivation, 469 validation cohort). Mean age was 65.7( $\pm$ 15) years, 704 (63.3%) were male. SRF occurred in 189/644 (29%) and 187/469 (40%) patients in derivation and validation cohort, respectively. At multivariate analysis, risk factors for SRF in the derivation cohort assessed at hospitalization were age  $\geq$ 70 years, obesity, body temperature  $\geq$ 38°C, RR  $\geq$ 22bpm, lymphocytes  $\leq$ 900/mm3, creatinine  $\geq$ 1 mg/dl, C-reactive protein  $\geq$ 10mg/dl, and lactate dehydrogenase  $\geq$ 350IU/L. Assigning points to each variable an individual risk score (PREDI-CO score) was obtained. At score of >3, sensitivity, specificity, positive and negative predictive values were 71.6%(65-79%), 89.1% (86-92%), 74%(67-80%), and 89%(85-91%), respectively; PREDI-CO score showed similar prognostic ability in the validation cohort. At score of >3, sensitivity, specificity, positive and negative predictive values were 80% (73-85%), 76 (70-81%), 69%(60-74%) and 85% (80-89%), respectively. PREDI-CO score can be useful to allocate resources and prioritize treatments during COVID-19 pandemic.

- 22. Development and validation of a model for individualized prediction of hospitalization risk in 4,536 patients with COVID-19. Jehi L, Ji X, Milinovich A, et al. PLoS One. 2020 Aug 11;15(8):e0237419. doi: 10.1371/journal.pone.0237419. eCollection 2020. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0237419 Findings: 4,536 patients tested positive for SARS-CoV-2 during the study period. Of those, 958 (21.1%) required hospitalization. By day 3 of hospitalization, 24% of patients were transferred to the intensive care unit, and around half of the remaining patients were discharged home. Ten patients died. Hospitalization risk was increased with older age, black race, male sex, former smoking history, diabetes, hypertension, chronic lung disease, poor socioeconomic status, shortness of breath, diarrhea, and certain medications (NSAIDs, immunosuppressive treatment). Hospitalization risk was reduced with prior flu vaccination. The online risk calculator is freely available and found at https://riskcalc.org/COVID19Hospitalization/. Our study crystallizes published risk factors of COVID-19 progression, but also provides new data on the role of social influencers of health, race, and influenza vaccination. In a context of a pandemic and limited healthcare resources, individualized outcome prediction through this nomogram or online risk calculator can facilitate complex medical decision-making.
- 23. Prior Routine Use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and Important Outcomes in Hospitalised Patients with COVID-19. Bruce E, Barlow-Pay F, Short R, et al. J Clin Med. 2020 Aug 10;9(8):E2586. doi: 10.3390/jcm9082586. <u>https://www.mdpi.com/2077-0383/9/8/2586/html</u>

Findings: This was a multicentre, observational study, with data collected from adult patients with COVID-19 admitted to eight UK hospitals. Of 1,222 patients eligible to be included, 54 (4.4%) were routinely prescribed NSAIDs prior to admission. Univariate results suggested a modest protective effect from the use of NSAIDs, but in the multivariable analysis, there was no association between prior NSAID use and time to mortality (adjusted HR (aHR) = 0.89, 95% CI 0.52-1.53, p = 0.67) or length of stay (aHR 0.89, 95% CI 0.59-1.35, p = 0.58). This study found no evidence that routine NSAID use was associated with higher COVID-19 mortality in hospitalised patients; therefore, patients should be advised to continue taking these medications until further evidence emerges. Our findings suggest that NSAID use might confer a modest benefit with regard to survival. However, as this finding was underpowered, further research is required.

 Distinct Early Serological Signatures Track with SARS-CoV-2 Survival. Atyeo C, Fischinger S, Zohar T, et al. *Immunity*. 2020 Jul 30:S1074-7613(20)30327-7. doi: 10.1016/j.immuni.2020.07.020. https://www.sciencedirect.com/science/article/pii/S1074761320303277 Findings: As SARS-CoV-2 infections and death counts continue to rise, it remains unclear why some individuals recover from infection, whereas others rapidly progress and die. Although the immunological mechanisms that underlie different clinical trajectories remain poorly defined, pathogen-specific antibodies often point to immunological mechanisms of protection. Here, we profiled SARS-CoV-2-specific humoral responses in a cohort of 22 hospitalized individuals. Despite inter-individual heterogeneity, distinct antibody signatures resolved individuals with different outcomes. Although no differences in SARS-CoV-2-specific IgG levels were observed, spike-specific humoral responses were enriched among convalescent individuals. Furthermore, this enriched immunodominant spike-specific antibody profile in convalescents was confirmed in a larger validation cohort. These results demonstrate that early antigen-specific and qualitative features of SARS-CoV-2-specific antibodies point to differences in disease trajectory, highlighting the potential importance of functional antigen-specific humoral immunity to guide patient care and vaccine development.

- 25. Obesity and Mortality Among Patients Diagnosed With COVID-19: Results from an Integrated Health Care Organization. Tartof SY, Qian L, Hong V, et al. *Ann Intern Med*. 2020 Aug 12. doi: 10.7326/M20-3742. <u>https://www.acpjournals.org/doi/10.7326/M20-3742</u> Findings: Among 6,916 patients with COVID-19, there was a J-shaped association between BMI and risk for death, even after adjustment for obesity-related comorbidities. Compared with patients with a BMI of 18.5 to 24 kg/m2, those with BMIs of 40 to 44 kg/m2 and greater than 45 kg/m2 had relative risks of 2.68 (95% CI, 1.43 to 5.04) and 4.18 (CI, 2.12 to 8.26), respectively. This risk was most striking among those aged 60 years or younger and men. Increased risk for death associated with Black or Latino race/ethnicity or other sociodemographic characteristics was not detected. Obesity plays a profound role in risk for death from COVID-19, particularly in male patients and younger populations. Our capitated system with more equalized health care access may explain the absence of effect of racial/ethnic and socioeconomic disparities on death.
- 26. Characteristics of peripheral blood differential counts in hospitalized patients with COVID-19. Pakos I, Lo KB, Salacup G, et al. *Eur J Haematol*. 2020 Aug 13. doi: 10.1111/ejh.13509. <u>https://onlinelibrary.wiley.com/doi/10.1111/ejh.13509</u>

Findings: Patients with COVID-19 who died had significantly lower median absolute monocyte count (AMC) (0.4 vs 0.5, p=0.039) and median platelet count (169 vs 213, p=0.009) compared to those who survived. Patients who died had a significantly higher neutrophil to lymphocyte ratio (6.4 vs 4.5, p = 0.001). The NLR was positively associated with death (OR=1.038; 95% CI, 1.003 to 1.074, p=0.031) while AMC was inversely associated with death (OR=0.200; 95% CI, 0.052 to 0.761, p=0.018). CONCLUSION: Among patients with COVID-19, a lower AMC and higher NLR are associated with higher mortality.

27. Hyperglycemia at Hospital Admission Is Associated with Severity of the Prognosis in Patients Hospitalized for COVID-19: The Pisa COVID-19 Study. Coppelli A, Giannarelli R, Aragona M, et al. *Diabetes Care*. 2020 Aug 11:dc201380. doi: 10.2337/dc20-1380. https://care.diabetesjournals.org/content/diacare/early/2020/08/07/dc20-1380.full.pdf Findings: Neutrophils were higher and lymphocytes and PaO2/FiO2 lower in HG than in DM and NG patients. DM and HG patients had higher D-dimer and worse inflammatory profile. Mortality was greater in HG (39.4% vs. 16.8%; unadjusted hazard ratio [HR] 2.20, 95% CI 1.27-3.81, P = 0.005) than in NG (16.8%) and marginally so in DM (28.6%; 1.73, 0.92-3.25, P = 0.086) patients. Upon multiple adjustments, only HG remained an independent predictor (HR 1.80, 95% CI 1.03-3.15, P = 0.04). After stratification by quintile of glucose levels, mortality was higher in quintile 4 (Q4) (3.57, 1.46-8.76, P = 0.005) and marginally in Q5 (29.6%) (2.32, 0.91-5.96, P = 0.079) vs. Q1. CONCLUSIONS: Hyperglycemia is an independent factor associated with severe prognosis in people hospitalized for COVID-19.

### 28. Sex differential in COVID-19 mortality varies markedly by age. Bhopal SS, Bhopal R. *Lancet.* August 13, 2020 DOI:https://doi.org/10.1016/S0140-6736(20)31748-7

https://www.sciencedirect.com/science/article/pii/S0140673620317487?via%3Dihub Findings: We examined the sex ratio through the life course to see if the COVID-19 mortality sex-differential was the same at every age. We analysed data collated by the National Institute for Demographic Studies from national statistical agencies across England and Wales, France, Germany, Italy, Netherlands, Portugal, Korea, and Spain from the beginning of the pandemic until June 21, 2020. Belgium and USA were not included due to presentation of data in different age categories. The overall male to female mortality sex ratio per 100 000 population was 1·4. This ratio was not equal at all ages. For example, for people aged 0–9 years the ratio was 0·81. The ratio was 1·9 in the 40–49 years age group, 2·3 in the 50–59 year age group, 2·6 in the 60– 69 years age group, and 1·65 in people older than 80 years. There was some variation across countries, although broadly the pattern was similar. These data alter our understanding of male–female differences; the relationship is not straightforward, and efforts should now be made to understand risk based on the interaction of sex and age, along with other factors.

#### Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a whole-population study. Barron E, Bakhai C, Kar P, et al. *Lancet Diabetes Endocrinol* 2020 Aug 13. DOI:https://doi.org/10.1016/S2213-8587(20)30272-2

https://www.thelancet.com/journals/landia/article/PIIS2213-8587(20)30272-2/fulltext Findings. Of the 61 414 470 individuals who were alive and registered with a general practice on Feb 16, 2020, 263 830 (0·4%) had a recorded diagnosis of type 1 diabetes, 2 864 670 (4·7%) had a diagnosis of type 2 diabetes, 41 750 (0·1%) had other types of diabetes, and 58 244 220 (94·8%) had no diabetes. 23 698 in-hospital COVID-19-related deaths occurred during the study period. A third occurred in people with diabetes: 7434 (31·4%) in people with type 2 diabetes, 364 (1·5%) in those with type 1 diabetes, and 69 (0·3%) in people with other types of diabetes. Unadjusted mortality rates per 100 000 people over the 72-day period were 27 (95% CI 27–28) for those without diabetes, 138 (124–153) for those with type 1 diabetes, and 260 (254–265) for those with type 2 diabetes. Adjusted for age, sex, deprivation, ethnicity, and geographical region, compared with people without diabetes, the odds ratios (ORs) for in-hospital COVID-19related death were 3·51 (95% CI 3·16–3·90) in people with type 1 diabetes and 2·03 (1·97–2·09) in people with type 2 diabetes. These effects were attenuated to ORs of 2·86 (2·58–3·18) for type 1 diabetes and 1·80 (1·75–1·86) for type 2 diabetes when also adjusted for previous hospital admissions with coronary heart disease, cerebrovascular disease, or heart failure. The results of this nationwide analysis in England show that type 1 and type 2 diabetes were both independently associated with increased odds of in-hospital death with COVID-19.

- 30. Mortality and Pre-Hospitalization use of Renin-Angiotensin System Inhibitors in Hypertensive COVID-19 Patients. Chen C, Wang F, Chen P, et al. J Am Heart Assoc. 2020 Aug 18;e017736. doi: 10.1161/JAHA.120.017736. <u>https://www.ahajournals.org/doi/10.1161/JAHA.120.017736</u> Findings: In a large single center retrospective analysis we observed a protective effect of prehospitalization use of RAS inhibitors on mortality in hypertensive COVID-19 patients; which might be associated with reduced inflammatory response.
- 31. Timing of Intubation and Mortality Among Critically III Coronavirus Disease 2019 Patients: A Single-Center Cohort Study. Hernandez-Romieu AC, Adelman MW, Hockstein MA, et al. *Crit Care Med.* 2020 Aug 14. doi: 10.1097/CCM.00000000004600. <u>https://journals.lww.com/ccmjournal/Abstract/9000/Timing of Intubation and Mortality Am</u> ong.95533.aspx

Findings: Among 231 patients admitted to the ICU, 109 (47.2%) were treated with high-flow nasal cannula and 97 (42.0%) were intubated without preceding high-flow nasal cannula use. Of those managed with high-flow nasal cannula, 78 (71.6%) ultimately received mechanical ventilation. Seventy-six patients (43.4%) were intubated within 8 hours of ICU admission, 57 (32.6%) between 8 and 24 hours of admission, and 42 (24.0%) greater than or equal to 24 hours after admission. Patients intubated within 8 hours were more likely to have diabetes, chronic comorbidities, and higher admission Sequential Organ Failure Assessment scores. Mortality did not differ by time to intubation ( $\leq 8$  hr: 38.2%; 8-24 hr: 31.6%;  $\geq 24$  hr: 38.1%; p = 0.7), and there was no association between time to intubation and mortality in adjusted analysis. In this cohort of critically ill patients with coronavirus disease 2019, neither time from ICU admission to intubation nor high-flow nasal cannula use were associated with increased mortality. This study provides evidence that coronavirus disease 2019 respiratory failure can be managed similarly to hypoxic respiratory failure of other etiologies.

32. Clinical characteristics and risk factors associated with COVID-19 severity in patients with haematological malignancies in Italy: a retrospective, multicentre, cohort study. Passamonti F, Cattaneo C, Arcaini L, et al. *Lancet Haematol.* 2020 Aug 13;S2352-3026(20)30251-9. doi: 10.1016/S2352-3026(20)30251-9.

https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(20)30251-9/fulltext Findings: Several small studies on patients with COVID-19 and haematological malignancies are available showing a high mortality in this population. We enrolled 536 patients with a median follow-up of 20 days at data cutoff, 85 (16%) of whom were managed as outpatients. 440 (98%) of 451 hospitalised patients completed their hospital course (were either discharged alive or died). 198 (37%) of 536 patients died. When compared with the general Italian population with COVID-19, the standardised mortality ratio was 2·04 in our whole study cohort and 3·72 in individuals younger than 70 years. When compared with the non-COVID-19 cohort with haematological malignancies, the standardised mortality ratio was 41·3. This study adds to the evidence that patients with haematological malignancies have worse outcomes than both the general population with COVID-19 and patients with haematological malignancies without COVID-19. The high mortality among patients with haematological malignancies hospitalised with COVID-19 highlights the need for aggressive infection prevention strategies, at least until effective vaccination or treatment strategies are available.

33. Chemotherapy and COVID-19 Outcomes in Patients with Cancer. Jee J, Foote MB, Lumish M, et al. J Clin Oncol. 2020 Aug 14; JCO2001307. doi: 10.1200/JCO.20.01307. https://ascopubs.org/doi/abs/10.1200/JCO.20.01307

Findings: We reviewed clinical characteristics and outcomes from patients with cancer and concurrent COVID-19 at Memorial Sloan Kettering Cancer Center until March 31, 2020 (n = 309), and observed clinical end points until April 13, 2020. Recent cytotoxic chemotherapy treatment was not associated with adverse COVID-19 outcomes. Patients with active hematologic or lung malignancies, peri-COVID-19 lymphopenia, or baseline neutropenia had worse COVID-19 outcomes. Interactions among antineoplastic therapy, cancer type, and COVID-19 are complex and warrant further investigation.

34. Association of Race with Mortality Among Patients Hospitalized With Coronavirus Disease **2019 (COVID-19) at 92 US Hospitals.** Yehia BR, Winegar A, Fogel R, et al. *JAMA Netw Open*. 2020;3(8):e2018039. doi:10.1001/jamanetworkopen.2020.18039

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/10.1001/jamanetworkopen.2 020.18039?utm source=For The Media&utm medium=referral&utm campaign=ftm links&ut m term=081820

Findings: Of 11,210 patients with confirmed COVID-19 presenting to hospitals, 4180 (37.3%) were Black patients and 5583 (49.8%) were men. The median age was 61 (46 to 74) years. Compared with White patients, Black patients were younger age, (66 years vs 61 years), were more likely to be women (2259 [49.0%] vs 2293 [54.9%]), were more likely to have Medicaid insurance (611 [13.3%] vs 1031 [24.7%]), and had higher median scores on the Neighborhood Deprivation Index and the Elixhauser Comorbidity Index. All-cause in-hospital mortality among hospitalized White and Black patients was 23.1% (724 of 3218) and 19.2% (540 of 2812), respectively. After adjustment for age, sex, insurance, comorbidities, neighborhood deprivation, and site of care, there was no statistically significant difference in risk of mortality between Black and White patients. Although current reports suggest that Black patients represent a disproportionate share of COVID-19 infections and death in the United States, in this study, mortality for those able to access hospital care did not differ between Black and White patients after adjusting for sociodemographic factors and comorbidities.

#### Survivorship & Rehabilitation

35. 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. August 18, 2020. 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.

#### Therapeutics

- 36. Extracorporeal Membrane Oxygenation for Patients with COVID-19 in Severe Respiratory Failure. Mustafa AK, Alexander PJ, Joshi DJ, et al. JAMA Surg. 2020 Aug 11. doi: 10.1001/jamasurg.2020.3950. <u>https://jamanetwork.com/journals/jamasurgery/fullarticle/2769429</u> Findings: The limited studies on patients with COVID-19 requiring ECMO have thus far demonstrated poor survival. Overall, this study demonstrates promising outcomes, with most patients alive and no longer receiving ventilator care and ECMO support and 73% discharged and no longer receiving oxygen. Complications have been minimal; there were no ischemic strokes, inotropic support, and tracheostomy requirements because of the early extubation strategy. Mortality was 15%.
- 37. SARS-CoV-2 Neutralizing Antibody Titers in Convalescent Plasma and Recipients in New Mexico: An Open Treatment Study in COVID-19 Patients. Bradfute SB, Hurwitz I, Yingling AV, et al. J Infect Dis. 2020 Aug 11:jiaa505. doi: 10.1093/infdis/jiaa505.

https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa505/5890960 Findings: NAb titers in the donor CP units were low (<1:40 to 1:160) and had no effect on recipient neutralizing activity one day after transfusion. NAb titers were detected in 6/12 patients upon enrollment and in 11/12 patients during at least two timepoints. Average titers peaked on day 7 and declined towards day 14 (P=0.004). NAb and IgG titers were correlated in donor plasma units ( $\rho$ =0.938, P<0.0001) and in the cumulative patient measures ( $\rho$ =0.781, P<0.0001). CONCLUSIONS: CP infusion did not alter recipient NAb titers. Pre-screening of CP may be necessary for selecting donors with high levels of neutralizing activity for infusion into patients with COVID-19.

38. Methylprednisolone as Adjunctive Therapy for Patients Hospitalized with COVID-19 (Metcovid): A Randomised, Double-Blind, Phase IIb, Placebo-Controlled Trial. Jeronimo CMP, Farias MEL, Val FFA, et al. *Clin Infect Dis.* 2020 Aug 12:ciaa1177. doi: 10.1093/cid/ciaa1177. <u>https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1177/5891816</u> FINDINGS: From April 18 to June 16, 2020, 647 patients were screened, 416 randomized, and 393 analyzed as mITT, MP in 194 and placebo in 199 individuals. SARS-CoV-2 infection was confirmed by RT-PCR in 81.3%. Mortality at day 28 was not different between groups. A subgroup analysis showed that patients over 60 years in the MP group had a lower mortality rate at day 28. Patients in the MP arm tended to need more insulin therapy, and no difference was seen in virus clearance in respiratory secretion until day 7. The findings of this study suggest that a short course of MP in hospitalized patients with COVID-19 did not reduce mortality in the overall population.

- 39. Safety of intermediate dose of low molecular weight heparin in COVID-19 patients. Mattioli M, Benfaremo D, Mancini M, et al. J Thromb Thrombolysis. 2020 Aug 13. doi: 10.1007/s11239-020-02243-z. https://link.springer.com/article/10.1007/s11239-020-02243-z Findings: To evaluate the safety of intermediate dose regimens of low-weight molecular heparin (LWMH) in COVID-19 patients with pneumonia, particularly in older patients. We retrospectively evaluated 105 hospitalized patients (61 M, 44 F; mean age 73.7 years) treated with subcutaneous enoxaparin: 80 mg/day in normal weight and mild-to-moderate impair or normal renal function; 40 mg/day in severe chronic renal failure or low bodyweight (< 45 kg); 100 mg/day if bodyweight was higher than 100 kg. All the patients had radiologically confirmed pneumonia and 63.8% had severe COVID-19. None of the patients had fatal haemorrhage; two (1.9%) patients had a major bleeding event (one spontaneous hematoma and one gastrointestinal bleeding). Only 6.7% of patients needed transfusions of red blood cells. One thrombotic event (pulmonary embolism) was observed. When compared to younger patients, patients older than 85 years had a higher mortality (40% vs 13.3%), but not an increased risk of bleeding or need for blood transfusion. The use of an intermediate dose of LWMH appears to be feasible and data suggest safety in COVID-19 patients, although further studies are needed.
- Impact of implementation of an individualised thromboprophylaxis protocol in critically ill ICU patients with COVID-19: A longitudinal controlled before-after study. Stessel B, Vanvuchelen C, Bruckers L, et al. *Thromb Res.* 2020 Jul 22;194:209-215. doi: 10.1016/j.thromres.2020.07.038. <u>https://www.thrombosisresearch.com/article/S0049-</u> 3848(20)30329-7/fulltext

Findings: Mortality, cumulative risk of VTE and need for CRRT may be significantly reduced in COVID-19 patients by implementation of a more aggressive thromboprophylaxis protocol. Future research should focus on confirmation of these results in a randomized design and on uncovering the mechanisms underlying these observations.

41. Hypermetabolism in critically ill patients with COVID-19 and the effects of hypothermia: A case series. Pey-JenYu, HughCassiere, KarlBocchieri, et al. *Metabolism Open*. September 2020 <a href="https://doi.org/10.1016/j.metop.2020.100046">https://doi.org/10.1016/j.metop.2020.100046</a>

https://www.sciencedirect.com/science/article/pii/S2589936820300268?via%3Dihub Findings: Mild hypothermia was applied on four critically ill patients with COVID-19 for 48 h. Metabolic rates, carbon dioxide production and oxygen consumption were measured by indirect calorimetry. The average resting energy expenditure (REE) was 299% of predicted. Mild hypothermia decreased the REE on average of 27.0% with resultant declines in CO2 production (VCO2) and oxygen consumption (VO2) by 29.2% and 25.7%, respectively. This decrease in VCO2 and VO2 was clinically manifested as improvements in hypercapnia (average of 19.1% decrease in pCO2 levels) and oxygenation (average of 50.4% increase in pO2). Our case series demonstrates the extent of hypermetabolism in COVID-19 critical illness and suggests that mild hypothermia reduces the metabolic rate, improves hypercapnia and hypoxia in critically ill patients with COVID-19.

42. Effect of Convalescent Plasma on Mortality among Hospitalized Patients with COVID-19: Initial Three-Month Experience. Joyner MJ et al. *medRxiv PREPRINT*. 2020.08.12.20169359; doi:

#### https://doi.org/10.1101/2020.08.12.20169359

#### https://www.medrxiv.org/content/10.1101/2020.08.12.20169359v1.full.pdf

Findings. Transfusion of convalescent plasma with higher antibody levels to hospitalized COVID-19 patients significantly reduced mortality compared to transfusions with low antibody levels. Transfusions within three days of COVID-19 diagnosis yielded greater reductions in mortality. Embedded in an Expanded Access Program providing access to COVID-19 convalescent plasma and designed to assess its safety, several signals consistent with efficacy of convalescent plasma in the treatment of hospitalized COVID-19 patients emerged.

# 43. Corticosteroid prevents COVID-19 progression within its therapeutic window: a multicenter, proof-of-concept, observational study. Li Y, Zhou X, Li T, et al. *Emerg Microbes Infect.* 2020 Aug 14;1-27. doi: 10.1080/22221751.2020.1807885.

https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1807885

Findings: Among a Shanghai cohort and a validation cohort, we enrolled COVID-19 patients showing marked radiographic progression. Short-term, low-to-moderate-dose corticosteroids were considered for them. After identifying the possible markers for the therapeutic window, we then divided the patients, based on whether they were treated with corticosteroids within the therapeutic window, into the early-start group and control group. We identified that the therapeutic window for corticosteroids was characterized by a marked radiographic progression and lactase dehydrogenase (LDH) less than two times the upper limit of normal (ULN). The proportion of patients requiring invasive mechanical ventilation was significantly lower in the early-start group than in the control group (10.6% vs. 33.3%, difference, 22.7%, 95% confidence interval [CI] 2.6% to 44.8%). Among the validation cohort of 51 patients, similar difference of the primary outcome was observed (45.0% vs. 74.2%, P=0.035). Among COVID-19 patients with marked radiologic progression, short-term, low-to-moderate-dose corticosteroids benefits patients with LDH levels of less than two times the ULN, who may be in the early phase of excessive inflammation.

#### Transmission / Infection Control

44. Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients. Lednicky JA, Lauzardo M, Fan ZH, et al. *medRiv PREPRINT*. August 4, 2020. doi:

https://doi.org/10.1101/2020.08.03.20167395

https://www.medrxiv.org/content/10.1101/2020.08.03.20167395v1

Findings: Air samples were collected in the room of two COVID-19 patients, one of whom had an active respiratory infection with a NP swab positive for SARS-CoV-2 by RT-qPCR. By using VIVAS air samplers that operate on a gentle water-vapor condensation principle, material was collected from room air and subjected to RT-qPCR and virus culture. The genomes of the SARS-CoV-2 collected from the air and of virus isolated in cell culture from air sampling and from a NP swab from a newly admitted patient in the room were sequenced. Findings - Viable virus was isolated from air samples collected 2 to 4.8m away from the patients. The genome sequence of the SARS-CoV-2 strain isolated from the material collected by the air samplers was identical to that isolated from the NP swab from the patient with an active infection. Estimates of viable viral concentrations ranged from 6 to 74 TCID50 units/L of air. Interpretation - Patients with respiratory manifestations of COVID-19 produce aerosols in the absence of aerosol-generating procedures that contain viable SARS-CoV-2, and these aerosols may serve as a source of transmission of the virus.

45. Impact of Extended Use and Decontamination with Vaporized Hydrogen Peroxide on N95 Respirator Fit. Lieu A, Mah J, Zanichelli V, et al. *Am J Infect Control.* 2020 Aug 14;S0196-6553(20)30775-6. doi: 10.1016/j.ajic.2020.08.010. <u>https://www.ajicjournal.org/article/S0196-</u> <u>6553(20)30775-6/pdf</u>

Findings: We investigated the impact of extended use and decontamination with VHP on N95 Respirator Fit. We performed a prospective cohort study to determine the number of times respirators can be decontaminated before respirator fit test failure. The primary outcome was the overall number of cycles required for half of the respirators to fail (either mechanical failure or fit test failure). 36 participants completed 360 hours of respirator usage across 90 cycles. The median number of cycles completed by participants before respirator failure was 2. The overall number of cycles required for half of respirators to fail was 1, 3, 5 and 4 for the 3M 1860(S), 3M 1870+, Moldex 151X and ProGear 88020 respirators, respectively. The combination of prolonged usage and VHP decontamination was associated with early failure. Decontamination and prolonged usage of respirators must be done cautiously.

46. Absence of nosocomial influenza and respiratory syncytial virus infection in the coronavirus disease 2019 (COVID-19) era: implication of universal masking in hospitals. Wong S, Lam GK, Ho-Yan C, et al. *Infect Control Hosp Epidemiol*. 2020 Aug 17;1-14. doi: 10.1017/ice.2020.425. https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/absence-of-nosocomial-influenza-and-respiratory-syncytial-virus-infection-in-the-coronavirus-disease-2019-covid19-era-implication-of-universal-masking-in-hospitals/B59AC6439A720BE3D012B0F3E1D7AC08

Findings: Universal masking for healthcare workers and patients in hospitals was adopted to combat COVID-19, with a compliance of 100% and 75.9% respectively. Zero nosocomial influenza A, influenza B, and respiratory syncytial virus infection was achieved from February to April 2020, which was significantly lower than the corresponding months in 2017-2019.

#### Vaccine

47. Phase 1/2 study of COVID-19 RNA vaccine BNT162b1 in adults. Mulligan MJ, Lyke KE, Kitchin N, et al. *Nature*. 2020 Aug 12. doi: 10.1038/s41586-020-2639-4.

https://www.nature.com/articles/s41586-020-2639-4 reference.pdf

Findings: We report the available safety, tolerability, and immunogenicity data from an ongoing placebo-controlled, observer-blinded dose escalation study among 45 healthy adults, 18 to 55 years of age, randomized to receive 2 doses, separated by 21 days, of 10  $\mu$ g, 30  $\mu$ g, or 100  $\mu$ g of BNT162b1, a lipid nanoparticle-formulated, nucleoside-modified mRNA vaccine that encodes trimerized SARS-CoV-2 spike glycoprotein receptor-binding domain (RBD). Local reactions and systemic events were dose-dependent, generally mild to moderate, and transient. A second vaccination with 100  $\mu$ g was not administered due to increased reactogenicity and a lack of meaningfully increased immunogenicity after a single dose compared to the 30  $\mu$ g dose. RBD-

binding IgG concentrations and SARS-CoV-2 neutralizing titers in sera increased with dose level and after a second dose. Geometric mean neutralizing titers reached 1.9- to 4.6-fold that of a panel of COVID-19 convalescent human sera at least 14 days after a positive SARS-CoV-2 PCR. These results support further evaluation of this mRNA vaccine candidate.

#### 48. Effect of an Inactivated Vaccine Against SARS-CoV-2 on Safety and Immunogenicity Outcomes: Interim Analysis of 2 Randomized Clinical Trials. Xia S, Duan K, Zhang Y, et al. JAMA. 2020 Aug 13. doi: 10.1001/jama.2020.15543.

https://jamanetwork.com/journals/jama/fullarticle/2769612

Findings: Among 320 patients who were randomized (mean age, 42.8 years; 200 women [62.5%]), all completed the trial up to 28 days after the whole-course vaccination. The 7-day adverse reactions occurred in 3 (12.5%), 5 (20.8%), 4 (16.7%), and 6 (25.0%) patients in the alum only, low-dose, medium-dose, and high-dose groups, respectively, in the phase 1 trial; and in 5 (6.0%) and 4 (14.3%) patients who received injections on days 0 and 14 for vaccine and alum only, and 16 (19.0%) and 5 (17.9%) patients who received injections on days 0 and 21 for vaccine and alum only, respectively, in the phase 2 trial. The most common adverse reaction was injection site pain, followed by fever, which were mild and self-limiting; no serious adverse reactions were noted. The geometric mean titers of neutralizing antibodies in the low-, medium-, and high-dose groups at day 14 after 3 injections were 316 (95% CI, 218-457), 206 (95% CI, 123-343), and 297 (95% CI, 208-424), respectively, in the phase 1 trial, and were 121 (95% CI, 95-154) and 247 (95% CI, 176-345) at day 14 after 2 injections in participants receiving vaccine on days 0 and 14 and on days 0 and 21, respectively, in the phase 2 trial. There were no detectable antibody responses in all alum-only groups. In this interim report of the phase 1 and phase 2 trials of an inactivated COVID-19 vaccine, patients had a low rate of adverse reactions and demonstrated immunogenicity; the study is ongoing. Efficacy and longer-term adverse event assessment will require phase 3 trials.

#### Whole Person Care

49. Challenges of Maintaining Optimal Nutritional Status in COVID-19 Patients in Intensive Care Settings. Minnelli N, Gibbs L, Larrivee J, et al. JPEN J Parenter Enteral Nutr. 2020 Aug 16. doi: 10.1002/jpen.1996. <u>https://onlinelibrary.wiley.com/doi/abs/10.1002/jpen.1996</u> Findings: Due to the novelty of COVID-19 disease, the situation is fluid and guidelines continue to be developed and updated. This article discusses the interim guidelines available for the nutrition support of ICU COVID-19 patients, and the challenges the critical care team and RDN may face from a nutrition standpoint.

#### Women & Children

50. Association between Youth Smoking, Electronic Cigarette Use, and Coronavirus Disease 2019. Gaiha SM, Cheng J, Halpern-Felsher B. *J Adolescent Health*. August 11,2020 DOI:https://doi.org/10.1016/j.jadohealth.2020.07.002 <u>https://www.jahonline.org/article/S1054-139X(20)30399-2/fulltext</u> Findings: COVID-19 diagnosis was five times more likely among ever-users of e-cigarettes only, seven times more likely among ever-dual-users, and 6.8 times more likely among past 30-day dual-users. Testing was nine times more likely among past 30-day dual-users and 2.6 times more likely among past 30-day e-cigarette only users. Symptoms were 4.7 times more likely among past 30-day dual-users.

51. Impact of Maternal SARS-CoV-2 Detection on Breastfeeding Due to Infant Separation at Birth. Popofsky S, Noor A, Leavens-Maurer J, et al. *J Pediatr*. 2020 Aug 10:S0022-3476(20)30986-0. doi: 10.1016/j.jpeds.2020.08.004. <u>https://www.jpeds.com/article/S0022-3476(20)30986-</u> <u>0/fulltext</u>

Findings: Of the 160 mother-newborn dyads, 103 mothers were reached by telephone, and 85 consented to participate. No significant difference was observed in pre-delivery feeding plan between the separated and unseparated dyads (P = .268). Higher rates of breastfeeding were observed in the unseparated dyads compared with the separated dyads in the hospital (p<0.001), and at home (p=0.012). In the setting of COVID-19, separation of mother-newborn dyads impacts breastfeeding outcomes, with lower rates of breastfeeding both during hospitalization and at home following discharge compared with unseparated mothers and infants. No evidence of vertical transmission was observed; one case of postnatal transmission occurred from an unmasked symptomatic mother who held her infant at birth.

52. Hospitalization Rates and Characteristics of Children Aged <18 Years Hospitalized with Laboratory-Confirmed COVID-19 - COVID-NET, 14 States, March 1-July 25, 2020. Kim L, Whitaker M, O'Halloran A, et al. *MMWR Morb Mortal Wkly Rep*. 2020 Aug 14;69(32):1081-1088. doi: 10.15585/mmwr.mm6932e3.

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https://www.cdc.gov/mmwr/volumes/69/wr/mm6932e3.htm
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Findings: During March 1-July 25, 2020, 576 pediatric COVID-19 cases were reported to the COVID-NET, a population-based surveillance system that collects data on laboratory-confirmed COVID-19-associated hospitalizations in 14 states. Based on these data, the cumulative COVID-19-associated hospitalization rate among children aged <18 years during March 1-July 25, 2020, was 8.0 per 100,000 population, with the highest rate among children aged <2 years (24.8). During March 21-July 25, weekly hospitalization rates steadily increased among children (from 0.1 to 0.4 per 100,000, with a weekly high of 0.7 per 100,000). Overall, Hispanic or Latino (Hispanic) and non-Hispanic black (black) children had higher cumulative rates of COVID-19associated hospitalizations (16.4 and 10.5 per 100,000, respectively) than did non-Hispanic white (white) children (2.1). Among 208 (36.1%) hospitalized children with complete medical chart reviews, 69 (33.2%) were admitted to an intensive care unit (ICU); 12 of 207 (5.8%) required invasive mechanical ventilation, and one patient died during hospitalization. Although the cumulative rate of pediatric COVID-19-associated hospitalization remains low (8.0 per 100,000 population) compared with that among adults (164.5), weekly rates increased during the surveillance period, and one in three hospitalized children were admitted to the ICU, similar to the proportion among adults.

- 53. Association between Number of In-Person Health Care Visits and SARS-CoV-2 Infection in Obstetrical Patients. Reale SC, Fields KG, Lumbreras-Marquez MI, et al. JAMA. August 14, 2020. doi:10.1001/jama.2020.15242 <u>https://jamanetwork.com/journals/jama/fullarticle/2769678</u> Findings: A major concern that has emerged from the coronavirus disease 2019 pandemic is patient avoidance of necessary medical care. There was no meaningful association between the number of in-person health care visits and the rate of SARS-CoV-2 infection in this sample of obstetrical patients in the Boston area. Massachusetts had the third highest SARS-CoV-2 infection rate in the country during the spring 2020 surge, and the Boston area was particularly affected. The findings from this obstetrical population who had frequent in-person visits to a health care setting and underwent universal testing for SARS-CoV-2 infection suggest in-person health care visits were not likely to be an important risk factor for infection and that necessary, in-person care can be safely performed.
- 54. Cardiac manifestations in SARS-CoV-2-associated multisystem inflammatory syndrome in children: a comprehensive review and proposed clinical approach. Sperotto F, Friedman KG, Son MF, et al. Eur J Pediatr. 2020 Aug 15. doi: 10.1007/s00431-020-03766-6. <a href="https://link.springer.com/content/pdf/10.1007/s00431-020-03766-6.pdf">https://link.springer.com/content/pdf/10.1007/s00431-020-03766-6.</a> https://link.springer.com/content/pdf/10.1007/s00431-020-03766-6.pdf Findings: What is Known: • Multisystem inflammatory syndrome in children (MIS-C) has been described associated with SARS-CoV-2. What is New: • Patients with MIS-C often present with fever, gastrointestinal symptoms, and shock. • Cardiac involvement is found in a high proportion of these patients, including ventricular dysfunction, coronary artery dilation or aneurysm, and arrhythmias. • Management is based on expert consensus and includes cardiac support, immunomodulatory agents, and anticoagulation. • Long-term follow-up is required due to the unclear prognosis and risk of progression of cardiac manifestation.</a>
- 55. Peripheral immunophenotypes in children with multisystem inflammatory syndrome associated with SARS-CoV-2 infection. Carter, M.J., Fish, M., Jennings, A. et al. *Nat Med* (2020). https://doi.org/10.1038/s41591-020-1054-6

Findings: Based on our cohort characteristics and the immune cell changes we observed, MIS-C is likely to be a distinct immunopathogenic illness associated with SARS-CoV-2, with more severe illness in seropositive children. The mechanisms underpinning these immune abnormalities are of priority for further research.

#### **GUIDELINES & CONSENSUS STATEMENTS**

AAP - <u>Children and COVID-19: State Data Report: A joint report from the American Academy of</u> <u>Pediatrics and the Children's Hospital Association</u>

#### AAP - Cloth Face Coverings

AAP - <u>Guidance on the Use of Personal Protective Equipment (PPE) for Pediatric Care in Ambulatory</u> <u>Care Settings during the SARS-CoV-2 Pandemic</u> Reducing Aerosol-Related Risk of Transmission in the Era of COVID-19: An Interim Guidance Endorsed by the International Society of Aerosols in Medicine. Fink JB, Ehrmann S, Li J, et al. J Aerosol Med Pulm Drug Deliv. 2020 Aug 12. doi: 10.1089/jamp.2020.1615.

FDA / CDC / NIH/ WHO Updates

CDC - <u>Guidance for General Laboratory Safety Practices during the COVID-19 Pandemic.</u> Updated August 15, 2020.

NIH - <u>Clinical Trials of Monoclonal Antibodies to Prevent COVID-19 Now Enrolling: Phase 3 Trials</u> <u>Conducted in the NIAID COVID-19 Prevention Network</u>

FDA - <u>Coronavirus (COVID-19) Update: FDA Issues Emergency Use Authorization to Yale School of</u> <u>Public Health for SalivaDirect, Which Uses a New Method of Saliva Sample Processing</u>

WHO - <u>Home care for patients with suspected or confirmed COVID-19 and management of their</u> <u>contacts</u>

**Commentary, News & Press Releases** 

Influenza in the COVID-19 Era. JAMA. 2020 Aug 14. doi: 10.1001/jama.2020.14661.

AAP - <u>American Academy of Pediatrics Tracks Children's COVID-19 Cases by State, Reflecting</u> <u>Increasing Cases</u>

Impact of the COVID-19 pandemic on clinical research. Tuttle KR. [*PSJH author*] Nat Rev Nephrol. 2020 Aug 5:1-3. doi: 10.1038/s41581-020-00336-9.

<u>US blacks 3 times more likely than whites to get COVID-19</u>. *State of Black America: Unmasked.* National Urban League.

Novavax Initiates Efficacy Trial of COVID-19 Vaccine in South Africa. August 17, 2020.

<u>Covid-19 Deaths Skew Younger Among Minorities</u>, according to a *Wall Street Journal* analysis of death-certificate data collected by federal authorities. August 16, 2020.

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