COVID-19 Resource Desk

#30 | 11.11.2020 to 11.17.2020

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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. **Characterization of pre-existing and induced SARS-CoV-2-specific CD8(+) T cells.** Schulien I, Kemming J, Oberhardt V, et al. *Nat Med.* 2020 Nov 12. doi: 10.1038/s41591-020-01143-2. https://www.nature.com/articles/s41591-020-01143-2
Findings: Emerging data indicate that SARS-CoV-2-specific CD8+ T cells targeting different viral proteins are detectable in up to 70% of convalescent individuals. However, very little information is currently available about the abundance, phenotype, functional capacity and fate of pre-existing and induced SARS-CoV-2-specific CD8+ T cell responses during the natural course of SARS-CoV-2 infection. Here, we define a set of optimal and dominant SARS-CoV-2-specific CD8+ T cell epitopes. We also perform a high-resolution ex vivo analysis of pre-existing and induced SARS-CoV-2-specific CD8+ T cells, applying peptide-loaded major histocompatibility complex class I (pMHCI) tetramer technology. We observe rapid induction, prolonged contraction and emergence of heterogeneous and functionally competent cross-reactive and induced memory CD8+ T cell responses in cross-sectionally analyzed individuals with mild disease following SARS-CoV-2 infection and three individuals longitudinally assessed for their T cells pre- and post-SARS-CoV-2 infection. SARS-CoV-2-specific memory CD8+ T cells exhibited functional characteristics comparable to influenza-specific CD8+ T cells and were detectable in SARS-CoV-2 convalescent individuals who were seronegative for anti-SARS-CoV-2 antibodies targeting spike (S) and nucleoprotein (N). These results define cross-reactive and induced SARS-CoV-2-specific CD8+ T cell responses as potentially important determinants of immune protection in mild SARS-CoV-2 infection.

2. **Immunological memory to SARS-CoV-2 assessed for greater than six months after infection.** Dan JM, Mateus J, Kato Y, et al. *bioRxiv PREPRINT* 2020.11.15.383323; doi: https://doi.org/10.1101/2020.11.15.383323
https://www.biorxiv.org/content/10.1101/2020.11.15.383323v1
Findings: Understanding immune memory to SARS-CoV-2 is critical for improving diagnostics and vaccines, and for assessing the likely future course of the pandemic. We analyzed multiple compartments of circulating immune memory to SARS-CoV-2 in 185 COVID-19 cases, including 41 cases at > 6 months post-infection. Spike IgG was relatively stable over 6+ months. Spike-

specific memory B cells were more abundant at 6 months than at 1 month. SARS-CoV-2-specific CD4+ T cells and CD8+ T cells declined with a half-life of 3-5 months. By studying antibody, memory B cell, CD4+ T cell, and CD8+ T cell memory to SARS-CoV-2 in an integrated manner, we observed that each component of SARS-CoV-2 immune memory exhibited distinct kinetics.

Clinical Syndrome

3. **Persistence and Evolution of SARS-CoV-2 in an Immunocompromised Host.** Choi B, Choudhary MC, Regan J, et al. *N Engl J Med*. 2020 Nov 11. doi: 10.1056/NEJMc2031364.
https://www.nejm.org/doi/full/10.1056/NEJMc2031364
Although most immunocompromised persons effectively clear SARS-CoV-2 infection, this case highlights the potential for persistent infection and accelerated viral evolution associated with an immunocompromised state.

4. **Exacerbation of neurological symptoms and COVID-19 severity in patients with preexisting neurological disorders and COVID-19: A systematic review.** Kubota T, Kuroda N. *Clin Neurol Neurosurg.* 2020 Nov 1:106349. doi: 10.1016/j.clineuro.2020.106349.
https://www.sciencedirect.com/science/article/pii/S0303846720306922
Findings: Twenty-six articles with 2278 patients with preexisting neurological disorder and COVID-19 were identified. Of 232 patients, 74 (31.9 %) showed exacerbation of preexisting neurological symptoms of dementia (55/92; 59.5 %), Parkinson's disease (10/17; 58.8 %), epilepsy (1/1; 100 %), and unspecified neurological disorders (8/106; 7.5 %). Of 2168 patients, 478 (22.0 %) showed severe COVID-19 course. These included patients with cerebrovascular disease (86/445; 19.3 %), dementia (70/316; 22.2 %), Parkinson's disease (25/214; 11.7 %), multiple sclerosis (28/71; 39.4 %), spinal cord injury (5/7; 71.4 %), epilepsy (10/98; 10.2 %) and unspecified neurological disorders (254/1011; 25 %). Patients with preexisting neurological disorders and COVID-19 may develop exacerbation of neurological symptoms and severe COVID-19. Clinicians should be aware of the risk of symptom exacerbation and severe COVID-19 in patients with preexisting neurological disease and should focus on the prevention and early care of COVID-19.

5. **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, Harrison PJ. *Lancet Psychiatry.* 2020 Nov 9:S2215-0366(20)30462-4. doi: 10.1016/S2215-0366(20)30462-4.
https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(20)30462-4/fulltext
FINDINGS: 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 (influenza; respiratory tract infections; skin infection; cholelithiasis; urolithiasis, and fracture of a large bone). The HR was greatest for anxiety disorders, insomnia, and dementia. The incidence of any psychiatric diagnosis in the 14 to 90 days after COVID-19 diagnosis was 18·1%, including 5·8% that were a first diagnosis. The incidence of a first diagnosis of dementia in the 14 to 90 days after COVID-19 diagnosis was 1·6% in people older than 65 years. A psychiatric diagnosis in the previous year was associated with a higher incidence of COVID-19 diagnosis. This risk was independent of known physical

health risk factors for COVID-19, but we cannot exclude possible residual confounding by socioeconomic factors. 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.

6. **Thrombosis in Hospitalized Patients with Viral Respiratory Infections versus COVID-19.**
   Smilowitz NR, Subashchandran V, Yuriditsky E, et al. *Am Heart J.* 2020 Nov 9:S0002-8703(20)30373-2. doi: 10.1016/j.ahj.2020.10.075.
   https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7654304/
   Findings: We evaluated the incidence of thrombosis in patients hospitalized with non-COVID-19 acute viral respiratory illnesses nationwide from 2012 to 2014 and compared this to the incidence among patients hospitalized with COVID-19 at a large health system in New York. Non-COVID-19 viral respiratory illness was complicated by acute MI in 2.8% of hospitalizations, VTE in 1.6%, ischemic stroke in 0.7%, and other systemic embolism in 0.1%. The proportion of hospitalizations complicated by thrombosis was lower in patients with viral respiratory illness in 2002-2014 than in COVID-19.

7. **Sleep Disordered Breathing Among Hospitalized Patients due to COVID-19.** Perger E, Soranna D, Pengo M, et al. *Am J Respir Crit Care Med.* 2020 Nov 12. doi: 10.1164/rccm.202010-3886LE.
   https://www.atsjournals.org/doi/pdf/10.1164/rccm.202010-3886LE
   Findings: A high rate of underdiagnosed SDB, in particular OSA, might act as cofactor in the elevated susceptibility for worse COVID-19 sequelae, independently of BMI. An appropriate assessment of SDB presence, type and severity in COVID-19 patients, also in the hospital setting, might thus favor a more accurate risk stratification and also help decision-making in therapeutic interventions. The possible role of SDB treatment in prognosis improvement of hospitalized patients for COVID-19 disease needs to be further investigated through properly sized intervention studies.

8. **Neurological manifestations associated with COVID-19: a multicentric registry.** Meppiel E, Peiffer-Smadja N, Maury A, et al. *Clin Microbiol Infect.* 2020 Nov 12:S1198-743X(20)30698-4. doi: 10.1016/j.cmi.2020.11.005.
   https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30698-4/fulltext
   Findings: We included 222 COVID-19 patients with neurological manifestations from 46 centers in France. Median age was 65 years, and 61.3% were male. COVID-19 was severe or critical in 102 patients (45.2%). The most common neurological diseases were COVID-19 associated encephalopathy (67/222, 30.2%), acute ischemic cerebrovascular syndrome (57/222, 25.7%), encephalitis (21/222, 9.5%), and Guillain-Barré Syndrome (15/222, 6.8%). Neurological manifestations appeared after first COVID-19 symptoms with a median (IQR) delay of 6 (3-8) days in COVID-19 associated encephalopathy, 7 (5-10) days in encephalitis, 12 (7-18) days in acute ischemic cerebrovascular syndrome and 18 (15-28) days in Guillain-Barré Syndrome. Brain imaging was performed in 192 patients (86.5%), including 157 MRI (70.7%). Among patients with acute ischemic cerebrovascular syndrome, 13/57 (22.8%) had multi territory ischemic strokes, with large vessel thrombosis in 16/57 (28.1%). Brain MRI of encephalitis

patients showed heterogeneous acute non vascular lesion in 14/21 patients (66.7%). Cerebrospinal fluid was analyzed in 97 patients (43.7%), with pleocytosis in 18 patients (18.6%) and a positive SARS-CoV-2 PCR in 2 patients with encephalitis. The median (IQR) follow-up was 24 (17-34) days with a high short-term mortality rate (28/222, 12.6%). Clinical spectrum and outcomes of neurological manifestations associated with SARS-CoV-2 infection were broad and heterogeneous, suggesting different underlying pathogenic processes.

9. **Low incidence of severe gastrointestinal complications in COVID-19 patients admitted to the intensive care unit: a large, multi-center study.** Qayed E, Deshpande AR, Elmunzer BJ; North American Alliance for the Study of Digestive Manifestation of COVID-19. *Gastroenterology*. 2020 Nov 11:S0016-5085(20)35397-X. doi: 10.1053/j.gastro.2020.11.009.
https://www.sciencedirect.com/science/article/pii/S001650852035397X
Findings: Patients hospitalized with COVID-19 often have gastrointestinal symptoms, including diarrhea, nausea, vomiting, and abdominal pain. However, the rate of gastrointestinal complications in patients with COVID-19 is less well described. Recent reports from a single center have suggested an alarmingly high rate of serious gastrointestinal complications in critically ill patients with COVID-19. In a retrospective review of 92 patients with severe COVID-19 admitted to the intensive care unit (ICU), 44 patients (48%) had ileus, 4 (4%) had intestinal ischemia, and 2 (2%) had Ogilvie syndrome. Several other case reports have described intestinal ischemia in the setting of COVID-19. However, reports from single centers should be interpreted with caution due to small sample sizes and limited generalizability to patients from wider geographic distributions. The aim of this study was to assess the rate of serious gastrointestinal complications in COVID-19 patients admitted to the ICU in a large, geographically diverse sample.

10. **Prevalence and characteristics of pulmonary embolism in 1042 COVID-19 patients with respiratory symptoms: A nested case-control study.** Planquette B, Le Berre A, Khider L, et al. *Thromb Res.* 2020 Nov 7;197:94-99. doi: 10.1016/j.thromres.2020.11.001.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7648521/
Findings: PE was suspected in 269 patients among 1042 COVID-19 patients and confirmed in 59 patients (5.6%). Half of PE was diagnosed at COVID-19 diagnosis. PE patients did not differ from CT and CTPA controls for thrombosis risk factors. PE patients more often required invasive ventilation compared to CTPA controls and to CT controls. PE patients exhibited more extensive parenchymal lesions (>50%) than CT controls. D-dimer levels were 5.1 (95% CI 1.90-13.76) times higher in PE patients than CTPA controls. Our results suggest a PE prevalence in COVID-19 patients close to 5% in the whole population and to 20% of the clinically suspected population. PE seems to be associated with more extensive lung damage and to require more frequently invasive ventilation.

11. **Acute Kidney Injury in a National Cohort of Hospitalized US Veterans with COVID-19.** Bowe B, Cai M, Xie Y, et al. *CJASN* November 2020, CJN.09610620; DOI:
https://doi.org/10.2215/CJN.09610620
Findings: In a cohort of 5216 US veterans hospitalized with COVID-19 identified through July 23, 2020, we described changes in serum creatinine and examined predictors of AKI and the

associations between AKI, health resource utilization, and death. In total, 1655 (32%) participants had AKI; 961 (58%), 223 (13%), and 270 (16%) met Kidney Disease Improving Global Outcomes definitions of stage 1, 2, and 3 AKI, respectively, and 201 (12%) received KRT. Eight percent of participants had AKI within 1 day of hospitalization, and 47% did not recover to baseline serum creatinine by discharge. Older age, Black race, male gender, obesity, diabetes, hypertension, and lower eGFR were significant predictors of AKI during hospitalization with COVID-19. AKI was associated with higher mechanical ventilation use (odds ratio, 6.46; 95% confidence interval, 5.52 to 7.57) and longer hospital stay (5.56 additional days; 95% confidence interval, 4.78 to 6.34). AKI was also associated with higher risk of death (odds ratio, 6.71; 95% confidence interval, 5.62 to 8.04); this association was stronger in Blacks (P value of interaction <0.001). Hospital-level rates of AKI exhibited substantial geographic variability, ranging from 10% to 56%. Between March and July 2020, AKI rates declined from 40% to 27%; proportions of AKI stage 3 and AKI requiring KRT decreased from 44% to 17%. Both geographic and temporal variabilities were predominately explained by percentages of Blacks (31% and 49%, respectively). AKI is common during hospitalization with COVID-19 and associated with higher risk of health care resource utilization and death. Nearly half of patients with AKI did not recover to baseline by discharge. Substantial geographic variation and temporal decline in rates and severity of AKI were observed.

Diagnostics & Screening

12. **Chembio DPP COVID-19 IgM/IgG Serological Testing: Laboratory Validation, Guidelines, and Recommendations.** Bardarov S, Cesare J, Kopolovich H, et al. *Clin Lab.* 2020 Nov 1;66(11). doi: 10.7754/Clin.Lab.2020.200850.
Findings: We evaluated the performance of Chembio serological test for IgM and IgG as an employee screening tool in a community hospital setting. The total number of currently asymptomatic employees screened was 1,866 from the Richmond University Medical Center. The non-exposed group included 1,253 (67.1%) employees with no significant clinical history and non-reactive IgM and IgG antibodies. The convalescent group included 255 (13.7%) of the employees with elevation of IgG only, 18 (1%) employees with past history of positive PCR and COVID-19 who currently have non-reactive IgM and IgG antibodies or demonstrate elevated IgG only, followed by 3 employees (< 1%) with no past clinical history who demonstrated reactive IgM and IgG antibodies and negative follow up by PCR. The reported 14.9% exposure/convalescent rate is lower than the reported 20% by the Department of Health and Governor Andrew Cuomo and may represent a better utilization of personal protective equipment, better hand washing techniques, and better disinfection procedures combined with strict social distancing. Chembio's performance is satisfactory; however, hospitals must design their own policies addressing: who needs to be screened and who will interpret the results as well as constructing management algorithms for employees with no previous history and current double positive antibodies.

13. **Assessment of SARS-CoV-2 RNA Test Results Among Patients Who Recovered From COVID-19 With Prior Negative Results.** Liotti FM, Menchinelli G, Marchetti S, et al. *JAMA Intern Med.* 2020 Nov 12. doi: 10.1001/jamainternmed.2020.7570.

https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/10.1001/jamainternmed.2020.7570
Findings: Some patients who have recovered from COVID-19 with documented negative RT-PCR results at the time of recovery have had subsequent positive RT-PCR test results for SARS-CoV-2 in the absence of any symptoms suggestive of new infection. It is unknown whether such patients are infectious and whether they should be quarantined. Real-time PCR is not a viral culture and does not allow determination of whether the virus is viable and transmissible. We investigated RT-PCR retested positive nasal/oropharyngeal swab (NOS) samples from recovered patients with COVID-19 with prior negative results for the presence of replicative SARS-CoV-2 RNA.

14. **Performance of Nucleic Acid Amplification Tests for Detection of Severe Acute Respiratory Syndrome Coronavirus 2 in Prospectively Pooled Specimens.** Wang H, Hogan CA, Miller JA, et al. *Emerg Infect Dis.* 2020 Nov 12;27(1). doi: 10.3201/eid2701.203379.
https://wwwnc.cdc.gov/eid/article/27/1/20-3379_article
Findings: Pooled nucleic acid amplification tests for severe acute respiratory syndrome coronavirus 2 could increase availability of testing at decreased cost. However, the effect of dilution on analytical sensitivity through sample pooling has not been well characterized. We tested 1,648 prospectively pooled specimens by using 3 nucleic acid amplification tests for severe acute respiratory syndrome coronavirus 2: a laboratory-developed real-time reverse transcription PCR targeting the envelope gene, and 2 commercially available Panther System assays targeting open reading frame 1ab. Positive percent agreement (PPA) of pooled versus individual testing ranged from 71.7% to 82.6% for pools of 8 and from 82.9% to 100.0% for pools of 4. We developed and validated an independent stochastic simulation model to estimate effects of dilution on PPA and efficiency of a 2-stage pooled real-time reverse transcription PCR testing algorithm. PPA was dependent on the proportion of tests with positive results, cycle threshold distribution, and assay limit of detection.

15. **Nucleic-acid-amplification tests from respiratory samples for the diagnosis of coronavirus infections: systematic review and meta-analysis.** Hellou MM, Górska A, Mazzaferri F, et al. *Clin Microbiol Infect*. 2020 Nov 11:S1198-743X(20)30695-9. doi: 10.1016/j.cmi.2020.11.002.
https://www.sciencedirect.com/science/article/pii/S1198743X20306959
Findings: Fifty-one studies were included; 22 including 10,181 persons before COVID-19 and 29 including 8,742 persons diagnosing SARS-CoV-2. The overall summary sensitivity was 89.1%, specificity 98.9%. Nearly all evaluated different PCRs both as index and reference standard. Real-time-RT PCR essays resulted in significantly higher sensitivity than other tests. Reference standards at high risk of bias possibly exaggerated specificity. The pooled sensitivity and specificity of studies evaluating SARS-COV-2 were 90.4% and 98.1%, respectively. SARS-COV-2 studies using lower respiratory tract samples, real-time RT-PCR and tests targeting the N, S or more than one gene showed higher sensitivity and RT-LAMP-based essays, especially when targeting only the RdRp gene, showed significantly lower sensitivity compared to other studies. Pooling all studies to date shows that about 10% of patients with coronavirus infections might be missed on average with PCR tests. Variables affecting sensitivity and specificity can be used for test selection and development.

Epidemiology & Public Health

16. **Susceptibility to Sars-COV-2 Infection among Children and Adults: A Seroprevalence Study of Family Households in the Barcelona Metropolitan Region, Spain.** Brotons P, Launes C, Buetas E, et al. *Clin Infect Dis.* 2020 Nov 12:ciaa1721. doi: 10.1093/cid/ciaa1721. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1721/5979490
Findings: A total of 381 family households including 381 first-reported PCR-positive adult cases and 1,084 contacts (672 children, 412 adults) were enrolled. SARS-CoV-2 infection seroprevalence rates were 17.6% (118/672) in children and 18.7% (77/335) in adult contacts (p=0.64). Among first-reported cases, seropositivity rates varied from 84.0% in adults previously hospitalized and tested within 6 weeks since the first positive PCR result to 31.5% in those not hospitalized and tested after that lag time (p<0.001). Nearly all (99.9%) positive pediatric contacts were asymptomatic or had mild symptoms. Children appear to have similar probability as adults to become infected by SARS-CoV-2 in quarantined family households but remain largely asymptomatic once infected. Adult antibody protection against SARS-CoV-2 seems to be weak at early convalescence and beyond 6 weeks post-infection confirmation, especially in cases that have experienced mild disease.

17. **Association between Ethnicity and Severe COVID-19 Disease: A Systematic Review and Meta-analysis.** Raharja A, Tamara A, Kok LT. *J Racial Ethn Health Disparities.* 2020 Nov 12. doi: 10.1007/s40615-020-00921-5.
Findings: Seventy-two articles (59 cohort studies with 17,950,989 participants, 13 ecological studies; 54 US-based, 15 UK-based; 41 peer-reviewed) were included for systematic review and 45 for meta-analyses. Risk of bias was low: median NOS 7 of 9. Compared to White ethnicity, unadjusted all-cause mortality was similar in Black and Asian but reduced in Hispanic ethnicity. Age- and sex-adjusted risks were significantly elevated for Black and Asian, but not for Hispanic. Further adjusting for comorbidities attenuated these associations to non-significance: Black; Asian; Hispanic. Subgroup analyses showed a trend towards greater disparity in outcomes for UK ethnic minorities, especially hospitalisation risk. This review could not confirm a certain ethnicity as an independent poor prognostic factor for COVID-19. Racial disparities in COVID-19 outcomes may be partially attributed to higher comorbidity rates in certain ethnicity.

18. **Mobility network models of COVID-19 explain inequities and inform reopening.** Chang S, Pierson E, Koh PW, et al. *Nature* 2020 Nov 10. https://www.nature.com/articles/s41586-020-2923-3
Findings: We introduce a metapopulation SEIR model that integrates fine-grained, dynamic mobility networks to simulate the spread of SARS-CoV-2 in 10 of the largest US metropolitan statistical areas. Derived from cell phone data, our mobility networks map the hourly movements of 98 million people from neighborhoods (census block groups, or CBGs) to points of interest (POIs) such as restaurants and religious establishments, connecting 57k CBGs to 553k POIs with 5.4 billion hourly edges. We show that by integrating these networks, a relatively simple SEIR model can accurately fit the real case trajectory, despite substantial changes in population behavior over time. Our model predicts that a small minority of

"superspreader" POIs account for a large majority of infections and that restricting maximum occupancy at each POI is more effective than uniformly reducing mobility. Our model also correctly predicts higher infection rates among disadvantaged racial and socioeconomic groups solely from differences in mobility: we find that disadvantaged groups have not been able to reduce mobility as sharply, and that the POIs they visit are more crowded and therefore higher-risk. By capturing who is infected at which locations, our model supports detailed analyses that can inform more effective and equitable policy responses to COVID-19.

19. **Impact of the COVID-19 Pandemic on Invasive Pneumococcal Disease and Risk of Pneumococcal Coinfection with SARS-CoV-2: prospective national cohort study, England.** Amin-Chowdhury Z, Aiano F, Mensah A, et al. *Clin Infect Dis.* 2020 Nov 16:ciaa1728. doi: 10.1093/cid/ciaa1728.
Findings: IPD incidence in 2019/20 was 30% lower compared to 2018/19 with large reductions observed across all age-groups during March-June 2020. The serotypes responsible for IPD during 2019/20 were similar to previous years. There were 160,886 SARS-CoV-2 and 1,137 IPD cases during February-June 2020, including 40 IPD/COVID-19 of SARS-CoV-2 infections. Large declines in IPD were observed following COVID-19 lockdown in England. IPD/COVID-19 confections were rare but associated with high CFR, mainly in older adults. The rarity, age distribution and serotype distribution of IPD/SARS-CoV-2 coinfections does not support wider extension of pneumococcal vaccination.

Healthcare Delivery & Healthcare Workers

20. **SARS-CoV-2 antibody prevalence in health care workers: Preliminary report of a single center study.** Michael Brant-Zawadzki, Deborah Fridman, Philip A Robinson, Matthew Zahn, Clayton Chau, Randy German, Marcus Breit, Jason R Bock, Junko Hara **[Hoag authors]**. *PLoS One*. 2020 Nov 12;15(11):e0240006. doi: 10.1371/journal.pone.0240006.
Findings: The present study reports on initial sero-surveillance conducted on healthcare workers at a regional hospital system in Orange County, California, during May and June, 2020. Study subjects were recruited from the entire hospital employee workforce and the independent medical staff. Data were collected for job duties and locations, COVID-19 symptoms, a PCR test history, travel record since January 2020, and existence of household contacts with COVID-19. A blood sample was collected from each subject for serum analysis for IgG antibodies to SARS-CoV-2. Of 2,992 tested individuals, a total 2,924 with complete data were included in the analysis. Observed prevalence of 1.06% (31 antibody positive cases), adjusted prevalence of 1.13% for test sensitivity and specificity were identified. Significant group differences between positive vs. negative were observed for age race, presence of fever, and loss of smell, but not for occupations. Possible explanation for this low prevalence includes a relatively low local geographic community prevalence (~4.4%) at the time of testing, the hospital's timely procurement of personal protective equipment, rigorous employee education, patient triage, and treatment protocol development and implementation.

21. **Factors affecting the mortality of patients with COVID-19 undergoing surgery and the safety of medical staff: A systematic review and meta-analysis.** Wang K, Wu C, Xu J, et al.

FINDINGS: A total of 269 patients from 47 studies were included in our meta-analysis. The mean age of operative patients with COVID-19 was 50.91 years, and 49% were female. A total of 28 patients were deceased, with the overall mortality of 6%. All deceased patients had postoperative complications associated with operation or COVID-19, including respiratory failure, acute respiratory distress syndrome (ARDS), short of breath, dyspnea, fever, cough, fatigue or myalgia, cardiopulmonary system, shock/infection, acute kidney injury and severe lymphopenia. Patients who presented any or more of the symptoms of respiratory failure, ARDS, short of breath and dyspnea after operation were associated with significantly higher mortality ($r = 0.891$, $p < 0.001$), while patients whose symptoms were presented as fever, cough, fatigue or myalgia only demonstrated marginally significant association with postoperative mortality ($r = 0.675$, $p = 0.023$). Twenty studies reported the information of medical staff infection, and a total of 38 medical staff were infected, and medical staff who used biosafety level 3 (BSL-3) protective equipment did not get infected. COVID-19 patients, in particular those with severe respiratory complications, may have high postoperative mortality. Medical staff in close contact with infected patients is suggested to take high level personal protective equipment.

22. **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.* 2020 Nov 13;69(45):1695-1699. doi:10.15585/mmwr.mm6945e2.
https://www.cdc.gov/mmwr/volumes/69/wr/mm6945e2.htm
Findings: Using electronic health record and administrative data from the Premier Healthcare Database,* CDC assessed patterns of hospital discharge, readmission, and demographic and clinical characteristics associated with hospital readmission after a patient's initial COVID-19 hospitalization (index hospitalization). Among 126,137 unique patients with an index COVID-19 admission during March-July 2020, 15% died during the index hospitalization. Among the 106,543 (85%) surviving patients, 9% (9,504) were readmitted to the same hospital within 2 months of discharge through August 2020. More than a single readmission occurred among 1.6% of patients discharged after the index hospitalization. Readmissions occurred more often among patients discharged to a skilled nursing facility (SNF) (15%) or those needing home health care (12%) than among patients discharged to home or self-care (7%). The odds of hospital readmission increased with age among persons aged ≥65 years, presence of certain chronic conditions, hospitalization within the 3 months preceding the index hospitalization, and if discharge from the index hospitalization was to a SNF or to home with health care assistance. These results support recent analyses that found chronic conditions to be significantly associated with hospital readmission and could be explained by the complications of underlying conditions in the presence of COVID-19, COVID-19 sequelae, or indirect effects of the COVID-19 pandemic. Understanding the frequency of, and risk factors for, readmission can inform clinical practice, discharge disposition decisions, and public health priorities such as health care planning to ensure availability of resources needed for acute and follow-up care of COVID-19 patients. With the recent increases in cases nationwide, hospital planning can account for these

increasing numbers along with the potential for at least 9% of patients to be readmitted, requiring additional beds and resources.

Laboratory Results

23. **Spike-specific circulating T follicular helper cell and cross-neutralizing antibody responses in COVID-19-convalescent individuals.** Zhang, J., Wu, Q., Liu, Z. et al. *Nat Microbiol* (2020). https://doi.org/10.1038/s41564-020-00824-5
Findings: Here, we show that the majority of COVID-19-convalescent individuals maintained SARS-CoV-2 spike S1- and S2-specific antibodies with neutralizing activity against the SARS-CoV-2 pseudotyped virus, and that some of the antibodies cross-neutralized SARS-CoV, Middle East respiratory syndrome coronavirus or both pseudotyped viruses. Convalescent individuals who experienced severe COVID-19 showed higher neutralizing antibody titres, a faster increase in lymphocyte counts and a higher frequency of CXCR3+ T follicular help (TFH) cells compared with COVID-19-convalescent individuals who experienced non-severe disease. Circulating TFH cells were spike specific and functional, and the frequencies of CXCR3+ TFH cells were positively associated with neutralizing antibody titres in COVID-19-convalescent individuals. No individuals had detectable autoantibodies. These findings provide insights into neutralizing antibody responses in COVID-19-convalescent individuals and facilitate the treatment and vaccine development for SARS-CoV-2 infection.

24. **Multi-Omics Resolves a Sharp Disease-State Shift between Mild and Moderate COVID-19.** Su Y, Chen D, Yuan D, et al. *Cell.* 2020 Oct 28:S0092-8674(20)31444-6. doi: 10.1016/j.cell.2020.10.037.
https://www.sciencedirect.com/science/article/pii/S0092867420314446
Findings: We present an integrated analysis of the clinical measurements, immune cells, and plasma multi-omics of 139 COVID-19 patients representing all levels of disease severity, from serial blood draws collected during the first week of infection following diagnosis. We identify a major shift between mild and moderate disease, at which point elevated inflammatory signaling is accompanied by the loss of specific classes of metabolites and metabolic processes. Within this stressed plasma environment at moderate disease, multiple unusual immune cell phenotypes emerge and amplify with increasing disease severity. We condensed over 120,000 immune features into a single axis to capture how different immune cell classes coordinate in response to SARS-CoV-2. This immune-response axis independently aligns with the major plasma composition changes, with clinical metrics of blood clotting, and with the sharp transition between mild and moderate disease. This study suggests that moderate disease may provide the most effective setting for therapeutic intervention.

25. **Proinflammatory IgG Fc structures in patients with severe COVID-19.** Chakraborty S, Gonzalez J, Edwards K, et al. *Nat Immunol.* 2020 Nov 9. doi: 10.1038/s41590-020-00828-7.https://www.nature.com/articles/s41590-020-00828-7
Findings: Here we show that patients with severe COVID-19 produced a unique serologic signature, including an increased likelihood of IgG1 with afucosylated Fc glycans. This Fc modification on severe acute respiratory syndrome coronavirus 2 IgGs enhanced interactions

with the activating Fcγ receptor FcγRIIIa; when incorporated into immune complexes, Fc afucosylation enhanced production of inflammatory cytokines by monocytes, including interleukin-6 and tumor necrosis factor. These results show that disease severity in COVID-19 correlates with the presence of proinflammatory IgG Fc structures, including afucosylated IgG1.

26. **Diaphragm Pathology in Critically Ill Patients with COVID-19 and Postmortem Findings From 3 Medical Centers.** Shi Z, de Vries HJ, Vlaar APJ, van der Hoeven J, Boon RA, Heunks LMA, Ottenheijm CAC; Dutch COVID-19 Diaphragm Investigators. *JAMA Intern Med.* 2020 Nov 16. doi: 10.1001/jamainternmed.2020.6278
Findings: In this study,we provide unique evidence forACE-2 expression in the human diaphragm and SARS-CoV-2 viral infiltration in the diaphragm of a subset of COVID-19–ICU patients. In COVID-19–ICU patients, we report increased expression of genes involved in fibrosis and histological evidence for the development of fibrosis in the diaphragm. This myopathic phenotype was distinctly different from that of control-ICU patients, with comparable duration of mechanical ventilation and ICU length of stay. It remains t obe established whether diaphragm myopathy is a direct effectof SARS-CoV-2. Only 3 patients in the control-ICU group (37.5%) had viral lung disease, and the association of viral pneumonia with diaphragm muscles is unknown. We hypothesize that severe diaphragm myopathy associated with COVID-19, as described in this study, may lead to diaphragm weakness and might contribute to ventilator weaning failure, persistent dyspnea, and fatigue in patients with COVID-19 who survive their ICU stay.

Prognosis

27. **Admission cardiac diagnostic testing with electrocardiography and troponin measurement prognosticates increased 30-day mortality in COVID-19.** Poterucha TJ, Elias P, Jain SS, et al. *J Am Heart Assoc.* 2020 Nov 10:e018476. doi: 10.1161/JAHA.120.018476.
https://www.ahajournals.org/doi/10.1161/JAHA.120.018476
Findings: We analyzed 887 patients (aged 64±17 years) admitted with COVID-19 from March 1 - April 3, 2020 in New York City with 12 lead ECG within 2 days of diagnosis. Demographics, comorbidities, and laboratory testing including high sensitivity cardiac troponin T (hs-cTnT) were abstracted. At 30 days follow-up, 556 patients (63%) were living without requiring mechanical ventilation, 123 (14%) were living and required mechanical ventilation, and 203 (23%) had expired. ECG findings included atrial fibrillation or atrial flutter (AF/AFL) in 46 (5%) and ST-T wave changes in 306 (38%). 27 (59%) patients with AF/AFL expired as compared to 181 (21%) of 841 with other non-life threatening rhythms (p<0.001). Multivariable analysis incorporating age, comorbidities, AF/AFL, QRS abnormalities, and ST-T wave changes, and initial hs-cTnT ≥ 20 ng/L showed that increased age (HR 1.04/year), elevated hs-cTnT (HR 4.57), AF/AFL (HR 2.07), and a history of coronary artery disease (HR 1.56) and active cancer (HR 1.87) were associated with increased mortality. Conclusions Myocardial injury with hs-cTnT ≥ 20 ng/L, in addition to cardiac conduction perturbations, especially AF/AFL, upon hospital admission for COVID-19 infection is associated with markedly increased risk for mortality than either diagnostic abnormality alone.

28. **Lack of association of antihypertensive drugs with the risk and severity of COVID-19: A meta-analysis.** Ren L, Yu S, Xu W, Overton JL, Chiamvimonvat N, Thai PN. *J Cardiol.* 2020 Nov 2:S0914-5087(20)30353-1. doi: 10.1016/j.jjcc.2020.10.015. https://www.journal-of-cardiology.com/article/S0914-5087(20)30353-1/fulltext

    Findings: We systematically searched PubMed, MEDLINE, The Cochrane Library, Cochrane Central Register of Controlled Trials (CENTRAL), ClinicalTrials.gov, and medRxiv for publications before July 13, 2020. Cohort studies and case-control studies that contain information on the association of antihypertensive agents including angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), calcium-channel blockers (CCBs), β-blockers, and diuretics with the risk and severity of COVID-19 were selected. The random or fixed-effects models were used to pool the odds ratio (OR) with 95% confidence interval (CI) for the outcomes. The literature search yielded 53 studies that satisfied our inclusion criteria, which comprised 39 cohort studies and 14 case-control studies. These studies included a total of 2,100,587 participants. We observed no association between prior usage of antihypertensive medications including ACEIs/ARBs, CCBs, β-blockers, or diuretics and the risk and severity of COVID-19. Additionally, when only hypertensive patients were included, the severity and mortality were lower with prior usage of ACEIs/ARBs. Taken together, usage of antihypertensive drugs is not associated with the risk and severity of COVID-19. Based on the current available literature, it is not recommended to abstain from the usage of these drugs in COVID-19 patients.

29. **The performance of the National Early Warning Score and National Early Warning Score 2 in hospitalised patients infected by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).** Kostakis I, Smith GB, Prytherch D, et al. *Resuscitation.* 2020 Nov 8:S0300-9572(20)30548-7. doi: 10.1016/j.resuscitation.2020.10.039. https://www.sciencedirect.com/science/article/pii/S0300957220305487

    Findings: NEWS or NEWS2 performance was good and similar in all five cohorts suggests that amendments to NEWS or NEWS2, such as the addition of new covariates or the need to change the weighting of existing parameters, are unnecessary when evaluating patients with COVID-19. Our results support the national and international recommendations for the use of NEWS or NEWS2 for the assessment of acute-illness severity in patients with COVID-19.

30. **Sixty-Day Outcomes Among Patients Hospitalized With COVID-19.** Chopra V, Flanders SA, O'Malley M, Malani AN, Prescott HC. *Ann Intern Med*. 2020 Nov 11. doi: 10.7326/M20-5661. https://www.acpjournals.org/doi/10.7326/M20-5661

    Findings: Of 1648 patients with COVID-19 admitted to 38 hospitals, 398 (24.2%) died during hospitalization and 1250 (75.8%) survived. Of 1250 patients discharged alive, 975 (78.0%) went home whereas 158 (12.6%) were discharged to a skilled nursing or rehabilitation facility (Table 1). By 60 days after discharge, an additional 84 patients (6.7% of hospital survivors and 10.4% of intensive care unit [ICU]-treated hospital survivors) had died, bringing the overall mortality rate for the cohort to 29.2%, and 63.5% for the 405 patients who received treatment in an ICU. Within 60 days of discharge, 189 patients (15.1% of hospital survivors) were rehospitalized.

31. **Do proton pump inhibitors influence SARS-CoV-2 related outcomes? A meta-analysis.** Li GF, An XX, Yu Y, et al. *Gut*. 2020 Nov 10:gutjnl-2020-323366. doi: 10.1136/gutjnl-2020-323366. https://gut.bmj.com/content/gutjnl/early/2020/11/10/gutjnl-2020-323366.full.pdf
Findings: Six studies including 318261 participants reported data on PPI usage and the risk of SARS-CoV-2 infection. Among them, five studies had information of current PPI users compared with nonusers and four on past PPI users versus non-users. Analysis of five studies encompassing 145428 patients who were tested for SARS-CoV-2 showed that the risk of SARS-CoV-2 infection was higher, although not significantly, among current PPI users compared with PPI non-users, with evidence of substantial between-study heterogeneity. Moreover, in a subgroup analysis of non-Korean cohorts, we found a significant association between current use of PPIs and increased risk of SARS-CoV-2 infection. Furthermore, a leave-one-out sensitivity analysis revealed that the summary estimate of the association between current PPI usage and SARS-CoV-2 infection was overly influenced by a single Korean study.

32. **Risk of severe COVID-19 disease with ACE inhibitors and angiotensin receptor blockers: cohort study including 8.3 million people.** Hippisley-Cox J, Tan PS, Coupland C. *Heart*. 2020 Nov 10:heartjnl-2020-318314. doi: 10.1136/heartjnl-2020-318314. https://heart.bmj.com/content/106/19/1503
Findings. Of 19 486 patients who had COVID-19 disease, 1286 received ICU care. ACE inhibitors were associated with a significantly reduced risk of COVID-19 disease but no increased risk of ICU care after adjusting for a wide range of confounders. There were significant interactions between ethnicity and ACE inhibitors and ARBs for COVID-19 disease. The risk of COVID-19 disease associated with ACE inhibitors was higher in Caribbean and Black African groups than the white group. A higher risk of COVID-19 with ARBs was seen for Black African than the white group. ACE inhibitors and ARBs are associated with reduced risks of COVID-19 disease after adjusting for a wide range of variables. Neither ACE inhibitors nor ARBs are associated with significantly increased risks of receiving ICU care. Variations between different ethnic groups raise the possibility of ethnic-specific effects of ACE inhibitors/ARBs on COVID-19 disease susceptibility and severity which deserves further study.

33. **Impact of heart failure on the clinical course and outcomes of patients hospitalized for COVID-19. Results of the Cardio-COVID-Italy multicentre study.** Tomasoni D, Inciardi RM, Lombardi CM, et al. *Eur J Heart Fail.* 2020 Nov 12. doi: 10.1002/ejhf.2052. https://onlinelibrary.wiley.com/doi/10.1002/ejhf.2052
Findings: We enrolled 692 consecutive patients admitted for COVID-19 in 13 Italian cardiology centres between 1st March and 9th April, 2020. Mean age was 67.4 ± 13.2 years, 69.5% patients were males, 90 (13.0%) had a history of HF, median hospitalization length was 14 days. In-hospital death occurred in 37 of 90 patients (41.1%) with HF history versus 126 of those with no HF history (20.9%). The increased risk of death associated with HF history remained significant after adjustment for clinical variables related to COVID-19 and HF severity, including comorbidities, oxygen saturation, lymphocyte count and plasma troponin. Hospitalized patients with COVID-19 and a history of HF have an extremely poor outcome with higher mortality and in-hospital complications. HF history is an independent predictor of increased in-hospital mortality. This article is protected by copyright. All rights reserved.

34. **Fibrosis-4 index as a predictor for mortality in hospitalised patients with COVID-19: a retrospective multicentre cohort study.** Park JG, Kang MK, Lee YR, et al. *BMJ Open.* 2020 Nov 12;10(11):e041989. doi: 10.1136/bmjopen-2020-041989.
https://bmjopen.bmj.com/content/10/11/e041989
Findings: Of the 1005 patients, 289 (28.8%) received respiratory support, and of these, 70 patients (24.2%) died. High fibrosis-4 index, low lymphocyte count, diabetes and systemic inflammatory response syndrome were found to be independent risk factors for mortality in patients with COVID-19 receiving respiratory support. Regardless of respiratory support, survival in the high FIB-4 group was significantly lower than in the low FIB-4 group (28.8 days vs 44.0 days). FIB-4 index is a useful predictive marker for mortality in patients with COVID-19 regardless of its severity.

35. **Identifying patients with symptoms suspicious for COVID-19 at elevated risk of adverse events: The COVAS score.** Sharp AL, Huang BZ, Broder B, et al. *Am J Emerg Med*. 2020 Nov 5:S0735-6757(20)30968-2. doi: 10.1016/j.ajem.2020.10.068.
https://www.ajemjournal.com/article/S0735-6757(20)30968-2/fulltext
Findings: 26,600 ED encounters were included and 1079 experienced an adverse event. Five categories (comorbidities, obesity/BMI ≥ 40, vital signs, age and sex) were included in the final score. The area under the curve (AUC) in the derivation cohort was 0.891 (95% CI, 0.880-0.901); similar performance was observed in the validation cohort (AUC = 0.895, 95% CI, 0.874-0.916). Sensitivity ranging from 100% (Score 0) to 41.7% (Score of ≥15) and specificity from 13.9% (score 0) to 96.8% (score ≥ 15). In the subgroups with pneumonia (n = 3252) the AUCs were 0.780 (derivation, 95% CI 0.759-0.801) and 0.832 (validation, 95% CI 0.794-0.870), while for COVID-19 diagnoses (n = 2059) the AUCs were 0.867 (95% CI 0.843-0.892) and 0.837 (95% CI 0.774-0.899) respectively. Physicians evaluating ED patients with pneumonia, COVID-19, or symptoms suspicious for COVID-19 can apply the COVAS score to assist with decisions to hospitalize or discharge patients during the SARS CoV-2 pandemic.

36. **Mortality and other adverse outcomes in patients with type 2 diabetes mellitus admitted for COVID-19 in association with glucose-lowering drugs: a nationwide cohort study.** Pérez-Belmonte LM, Torres-Peña JD, López-Carmona MD, et al. *BMC Med.* 2020 Nov 16;18(1):359. doi: 10.1186/s12916-020-01832-2.
Findings: A total of 2666 patients were found in the SEMI-COVID-19 Registry, 1297 on glucose-lowering drugs in monotherapy and 465 in combination with metformin. After propensity matching, 249 patients on metformin, 105 on dipeptidyl peptidase-4 inhibitors, 129 on insulin, 127 on metformin/dipeptidyl peptidase-4 inhibitors, 34 on metformin/sodium-glucose cotransporter 2 inhibitor, and 67 on metformin/insulin were selected. No at-home glucose-lowering drugs showed a significant association with in-hospital death; the composite outcome of the need of intensive care unit admission, mechanical ventilation, or in-hospital death; in-hospital complications; or long-time hospital stays. Given the close relationship between diabetes and COVID-19 and the limited evidence on the role of glucose-lowering drugs, prospective studies are needed.

Survivorship & Rehabilitation

37. **'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19.** Mandal S, Barnett J, Brill SE, et al. *Thorax.* 2020 Nov 10:thoraxjnl-2020-215818. doi: 10.1136/thoraxjnl-2020-215818.
https://thorax.bmj.com/content/early/2020/11/09/thoraxjnl-2020-215818
Findings: Large numbers of people are being discharged from hospital following COVID-19 without assessment of recovery. In 384 patients (mean age 59.9 years; 62% male) followed a median 54 days post discharge, 53% reported persistent breathlessness, 34% cough and 69% fatigue. 14.6% had depression. In those discharged with elevated biomarkers, 30.1% and 9.5% had persistently elevated d-dimer and C reactive protein, respectively. 38% of chest radiographs remained abnormal with 9% deteriorating. Systematic follow-up after hospitalisation with COVID-19 identifies the trajectory of physical and psychological symptom burden, recovery of blood biomarkers and imaging which could be used to inform the need for rehabilitation and/or further investigation.

38. **Disparities in Post-Intensive Care Syndrome During the COVID-19 Pandemic: Challenges and Solutions.** Moses J.E. Flash, BA, Shawn F. et al. *NEJM Catalyst*. November 13, 2020
https://catalyst.nejm.org/doi/full/10.1056/CAT.20.0568
Findings: Patients recovering from Covid-19 are at risk for a host of physical, cognitive, and psychiatric sequelae of critical illness, collectively termed "post-intensive care syndrome (PICS)." In the present article, we review the literature on disparities in PICS, highlight the personal toll of Covid-19 on our patients, and suggest solutions to anticipated challenges. We outline a three-pronged approach involving (1) the prevention of critical illness, (2) the deployment of short-term post-hospitalization initiatives, and (3) the implementation of long-term post-hospitalization and community-based solutions.

Therapeutics

39. **Early, low-dose, short-term methylprednisolone decreased the mortality in critical COVID-19 patients: a multicenter retrospective cohort study.** Ji J, Wu M, Zhong L, et al. *J Infect*. 2020 Nov 8:S0163-4453(20)30696-4. doi: 10.1016/j.jinf.2020.11.001.
https://www.journalofinfection.com/article/S0163-4453(20)30696-4/fulltext
Findings: Present study aimed to evaluate the effect of GC on different patient population. Since critical patients were more likely to receive GC therapy, only severe type and critical type patients, according to clinical classification of the Chinese Recommendations for Diagnosis and Treatment of Novel Coronavirus (SARSCoV2) infection (Trial 7th version), were enrolled in present study. We retrospective collected the clinical and outcome data of critical COVID-19 patients, and taking methylprednisolone (MP) treatment, the most used GC during clinical treatment, as an exposure factor analyzed the outcome. This study provides information on MP clinical application in treatment of SARS-CoV-2 infection, including patient selection and administration time and dosage.

40. **Fluvoxamine vs Placebo and Clinical Deterioration in Outpatients with Symptomatic COVID-19: A Randomized Clinical Trial.** Lenze EJ, Mattar C, Zorumski CF, et al. *JAMA*. November 12, 2020. doi:10.1001/jama.2020.22760
https://jamanetwork.com/journals/jama/fullarticle/2773108?resultClick=1
Findings: In this randomized trial that included 152 adult outpatients with confirmed COVID-19 and symptom onset within 7 days, clinical deterioration occurred in 0 patients treated with fluvoxamine vs 6 (8.3%) patients treated with placebo over 15 days, a difference that was statistically significant. In this preliminary study, adult outpatients with symptomatic COVID-19 treated with fluvoxamine, compared with placebo, had a lower likelihood of clinical deterioration over 15 days; however, determination of clinical efficacy would require larger randomized trials with more definitive outcome measures.

41. **Corticosteroid therapy for coronavirus disease 2019-related acute respiratory distress syndrome: a cohort study with propensity score analysis.** Wu C, Hou D, Du C, et al. *Crit Care.* 2020 Nov 10;24(1):643. doi: 10.1186/s13054-020-03340-4.
https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-03340-4
Findings: A total of 382 patients [60.7 ± 14.1 years old, 61.3% males] were analyzed. The median of sequential organ failure assessment (SOFA) score was 2.0 (IQR 2.0-3.0). Of these cases, 94 (24.6%) patients had invasive mechanical ventilation. The number of patients received systemic corticosteroids was 226 (59.2%), and 156 (40.8%) received standard treatment. The maximum dose of corticosteroids was 80.0 (IQR 40.0-80.0) mg equivalent methylprednisolone per day, and duration of corticosteroid treatment was 7.0 (4.0-12.0) days in total. In Cox regression analysis using corticosteroid treatment as a time-varying variable, corticosteroid treatment was associated with a significant reduction in risk of in-hospital death within 60 days after adjusting for age, sex, SOFA score at hospital admission, propensity score of corticosteroid treatment, comorbidities, antiviral treatment, and respiratory supports (HR 0.42; 95% CI 0.21, 0.85; p = 0.0160). Corticosteroids were not associated with delayed viral RNA clearance in our cohort. In this clinical practice setting, low-dose corticosteroid treatment was associated with reduced risk of in-hospital death within 60 days in COVID-19 patients who developed ARDS.

42. **Randomized Controlled Open Label Trial on the Use of Favipiravir Combined with Inhaled Interferon beta-1b in Hospitalized Patients with Moderate to Severe COVID-19 Pneumonia.** Khamis F, Al Naabi H, Al Lawati A, et al. *Int J Infect Dis*. 2020 Nov 9:S1201-9712(20)32319-5. doi: 10.1016/j.ijid.2020.11.008.
https://www.sciencedirect.com/science/article/pii/S1201971220323195
Findings: A total of 89 patients underwent randomization with 49% (n = 44) assigned to favipiravir and 51% (n = 45) assigned HCQ. The overall mean age was 55 ± 14 years and 58% (n = 52) were males. There were no significant differences in the inflammatory biomarkers at hospital discharge between the two groups. There were also no significant differences between the two groups with regards to the overall LOS, transfers to the ICU, discharges and overall mortality. No differences in clinical outcomes were found between favipiravir plus inhaled interferon beta-1b and hydroxychloroquine in adults hospitalized with moderate to severe COVID-19 pneumonia.

43. **Safety and efficacy of inhaled nebulised interferon beta-1a (SNG001) for treatment of SARS-CoV-2 infection: a randomised, double-blind, placebo-controlled, phase 2 trial.** Monk PD et al. *Lancet Respir Med* 2020 Nov 12. DOI:https://doi.org/10.1016/S2213-2600(20)30511-7
https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30511-7/fulltext
Findings: Between March 30 and May 30, 2020, 101 patients were randomly assigned to SNG001 (n=50) or placebo (n=51). 48 received SNG001 and 50 received placebo and were included in the intention-to-treat population. 66 (67%) patients required oxygen supplementation at baseline: 29 in the placebo group and 37 in the SNG001 group. Patients receiving SNG001 had greater odds of improvement on the OSCI scale (odds ratio 2·32 [95% CI 1·07–5·04]; p=0·033) on day 15 or 16 and were more likely than those receiving placebo to recover to an OSCI score of 1 (no limitation of activities) during treatment (hazard ratio 2·19 [95% CI 1·03–4·69]; p=0·043). SNG001 was well tolerated. The most frequently reported treatment-emergent adverse event was headache (seven [15%] patients in the SNG001 group and five [10%] in the placebo group). There were three deaths in the placebo group and none in the SNG001 group. Patients who received SNG001 had greater odds of improvement and recovered more rapidly from SARS-CoV-2 infection than patients who received placebo, providing a strong rationale for further trials.

44. **Effectiveness and safety of intravenous tocilizumab to treat COVID-19-associated hyperinflammatory syndrome: Covizumab-6 observational cohort.** Corominas H, Castellví I, Pomar V, et al. *Clin Immunol.* 2020 Nov 12:108631. doi: 10.1016/j.clim.2020.108631.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7658611/
Findings: Although the starting event in COVID-19 is a viral infection some patients present with an over-exuberant inflammatory response, leading to acute lung injury (ALI) and adult respiratory distress syndrome (ARDS). Since IL-6 plays a critical role in the inflammatory response, we assessed the efficacy and safety of tocilizumab (TCZ) in this single-centre, observational study in all Covid-19 in-patient with a proven SARS-CoV-2 rapidly progressing infection to prevent ALI and ARDS. 104 patients with COVID-19 treated with TCZ had a lower mortality rate (5·8%) compared with the regional mortality rate (11%), hospitalized patient's mortality (10%), and slightly lower than hospitalized patients treated with our standard of care alone (6%). We found that TCZ rapidly decreased acute phase reactants, ferritin and liver release of proteins. D-Dimer decreased slowly. We did not observe specific safety concerns. Early administration of IL6-R antagonists in COVID-19 patients with impending hyperinflammatory response, may be safe and effective treatment to prevent, ICU admission and further complications.

Transmission / Infection Control

45. **Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans.** Oude Munnink BB, Sikkema RS, Nieuwenhuijse DF, et al. *Science.* 2020 Nov 10:eabe5901. doi: 10.1126/science.abe5901.
https://science.sciencemag.org/content/early/2020/11/09/science.abe5901
Findings: Here, we describe an in-depth investigation using whole genome sequencing of outbreaks on 16 mink farms and the humans living or working on these farms. We conclude

that the virus was initially introduced from humans and has since evolved, most likely reflecting widespread circulation among mink in the beginning of the infection period several weeks prior to detection. Despite enhanced biosecurity, early warning surveillance and immediate culling of infected farms, transmission occurred between mink farms in three big transmission clusters with unknown modes of transmission. Sixty-eight percent (68%) of the tested mink farm residents, employees and/or contacts had evidence of SARS-CoV-2 infection. Where whole genomes were available, these persons were infected with strains with an animal sequence signature, providing evidence of animal to human transmission of SARS-CoV-2 within mink farms.

46. **SARS-CoV-2 Transmission among Marine Recruits during Quarantine.** Letizia AG et al. *NEJM* 2020 Nov 11. DOI: 10.1056/NEJMoa2029717
https://www.nejm.org/doi/full/10.1056/NEJMoa2029717
Findings: A total of 1848 recruits volunteered to participate in the study; within 2 days after arrival on campus, 16 (0.9%) tested positive for SARS-CoV-2, 15 of whom were asymptomatic. An additional 35 participants (1.9%) tested positive on day 7 or on day 14. Five of the 51 participants (9.8%) who tested positive at any time had symptoms in the week before a positive qPCR test. Of the recruits who declined to participate in the study, 26 (1.7%) of the 1554 recruits with available qPCR results tested positive on day 14. No SARS-CoV-2 infections were identified through clinical qPCR testing performed as a result of daily symptom monitoring. Analysis of 36 SARS-CoV-2 genomes obtained from 32 participants revealed six transmission clusters among 18 participants. Epidemiologic analysis supported multiple local transmission events, including transmission between roommates and among recruits within the same platoon. Among Marine Corps recruits, approximately 2% who had previously had negative results for SARS-CoV-2 at the beginning of supervised quarantine, and less than 2% of recruits with unknown previous status, tested positive by day 14. Most recruits who tested positive were asymptomatic, and no infections were detected through daily symptom monitoring. Transmission clusters occurred within platoons. (Funded by the Defense Health Agency and others.)
> *See also*: **An Outbreak of Covid-19 on an Aircraft Carrier.** Kasper MR et al. NEJM 2020 Nov 11. DOI: 10.1056/NEJMoa2019375

47. **Facemasks and the Cardiorespiratory Response to Physical Activity in Health and Disease.** Hopkins SR, Dominelli PB, Davis CK, et al. *Ann Am Thorac Soc.* 2020 Nov 16. doi: 10.1513/AnnalsATS.202008-990CME.
Findings: We review the literature on the effects of various facemasks and respirators on the respiratory system during physical activity using data from several models: cloth face coverings and surgical masks, N95 respirators, industrial respirators and applied high resistive or high deadspace respiratory loads. Overall, the available data suggest that although dyspnea may be increased and alter perceived effort with activity, the effects on Wb, blood gases and other physiological parameters imposed by facemasks during physical activity are small, often too small to be detected, even during very heavy exercise. There is no current evidence to support sex-based or age-based differences in the physiological responses to exercise while wearing a facemask. While the available data suggest that negative effects of using cloth or surgical

facemasks during physical activity in healthy individuals are negligible and unlikely to impact exercise tolerance significantly, for some individuals with severe cardiopulmonary disease, any added resistance and/or minor changes in blood gases may evoke considerably more dyspnea and, thus, affect exercise capacity.

Women & Children

48. **COVID-19 pandemic effect on early pregnancy: are miscarriage rates altered, in asymptomatic women?** Rotshenker-Olshinka K, Volodarsky-Perel A, Steiner N, et al. *Arch Gynecol Obstet.* 2020 Nov 9. doi: 10.1007/s00404-020-05848-0. https://link.springer.com/article/10.1007/s00404-020-05848-0
Findings: 113 women came for a first-trimester viability scan in the study period, and 172 in the control period (5-11 weeks gestational age), mean maternal age 36.5 ± 4.5 and 37.2 ± 5.4 years (p = 0.28). Viable clinical pregnancy rate was not different between the two groups (76.1 vs. 80.2% in the pandemic and pre-pandemic groups p = 0.41). No significant difference was seen in the total number of arrested pregnancies (defined as the sum of biochemical, 1st trimester miscarriages, and blighted ova) (22.1 vs. 16.9% p = 0.32), or in each type of miscarriage. The COVID-19 pandemic environment does not seem to affect early first-trimester miscarriage rates in asymptomatic patients.

49. **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. *Lancet Child Adolesc Health.* 2020 Nov 9:S2352-4642(20)30342-4. doi: 10.1016/S2352-4642(20)30342-4. https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30342-4/fulltext
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 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.

50. **Immunological assessment of pediatric multisystem inflammatory syndrome related to COVID-19.** Grazioli S, Tavaglione F, Torriani G, et al. *J Pediatric Infect Dis Soc.* 2020 Nov

12:piaa142. doi: 10.1093/jpids/piaa142. https://academic.oup.com/jpids/advance-article/doi/10.1093/jpids/piaa142/5979492

Findings: RT-PCRs on multiple anatomical compartments were negative whereas anti-SARS-CoV-2 IgA and IgG were strongly positive by ELISA and immunofluorescence. Both pseudo- and full virus neutralization assays showed the presence of neutralizing antibodies in all children, confirming a recent infection with SARS-CoV-2. Analyses of cytokine profiles revealed an elevation in all cytokines, as reported in adults with severe COVID-19. Although differing in clinical presentation, some features of MIS-C show phenotypic overlap with haemophagocytic lymphohistiocytosis (HLH). In contrast to patients with primary HLH, our patients showed normal perforin expression and NK cell degranulation. The levels of soluble IL-2 receptor (sIL-2R) correlated with the severity of disease, reflecting recent T-cell activation. Our findings suggest that MIS-C related to COVID-19 is caused by a post-infectious inflammatory syndrome associated with elevation in all cytokines, and markers of recent T-cell activation (sIL-2R) occurring despite a strong and specific humoral response to SARS-CoV2. Further functional and genetic analyses are essential to better understand the mechanisms of host-pathogen interactions.

51. **Mental Health–Related Emergency Department Visits among Children Aged <18 Years During the COVID-19 Pandemic — United States, January 1–October 17, 2020.** Leeb RT, Bitsko RH, Radhakrishnan L, et al. *MMWR Morb Mortal Wkly Rep* 2020;69:1675–1680. DOI: http://dx.doi.org/10.15585/mmwr.mm6945a3

Findings: Beginning in April 2020, the proportion of children's mental health–related ED visits among all pediatric ED visits increased and remained elevated through October. Compared with 2019, the proportion of mental health–related visits for children aged 5–11 and 12–17 years increased approximately 24%. and 31%, respectively. Monitoring indicators of children's mental health, promoting coping and resilience, and expanding access to services to support children's mental health are critical during the COVID-19 pandemic.

52. **SARS-CoV-2 Clinical Syndromes and Predictors of Disease Severity in Hospitalized Children and Youth.** Tri-State Pediatric COVID-19 Research Consortium Authors. *J Pediatr*. 2020 Nov 13:S0022-3476(20)31393-7. doi: 10.1016/j.jpeds.2020.11.016.

Findings: We identified 281 hospitalized patients with SARS-CoV-2 infections and divided them into three groups based on clinical features. Overall, 143 (51%) had respiratory disease, 69 (25%) had MIS-C, and 69 (25%) had other manifestations including gastrointestinal illness or fever. Patients with MIS-C were more likely to identify as non-Hispanic black compared with patients with respiratory disease. Seven patients (2%) died and 114 (41%) were admitted to the ICU. Obesity and hypoxia on admission were predictive of severe respiratory disease. Lower absolute lymphocyte count and higher C-reactive protein were predictive of severe MIS-C. Race/ethnicity or socioeconomic status were not predictive of disease severity.

53. **Pandemics, epidemics and inequities in routine childhood vaccination coverage: a rapid review.** Spencer N, Nathawad R, Arpin E, Johnson S. *BMJ Paediatr Open.* 2020 Nov 2;4(1):e000842. doi: 10.1136/bmjpo-2020-000842.

Findings: We conducted a rapid review of the impact of pandemics on existing inequities in routine vaccination coverage. PICO search framework: Population: children 0-18 years; Intervention/exposure: pandemic/epidemic; Comparison: inequality; Outcome: routine vaccination coverage. The review demonstrates a gap in the literature as none of the 29 papers selected for full-paper review from 1973 abstracts identified from searches met the inclusion criteria.

GUIDELINES & CONSENSUS STATEMENTS

Consensus-based clinical recommendations and research priorities for anticoagulant thromboprophylaxis in children hospitalized for COVID-19-related illness. Goldenberg NA, Sochet A, Albisetti M, et al. *J Thromb Haemost*. 2020 Nov;18(11):3099-3105. doi: 10.1111/jth.15073. https://onlinelibrary.wiley.com/doi/10.1111/jth.15073

FDA / CDC / NIH / WHO Updates

CDC - Scientific Brief: Community Use of Cloth Masks to Control the Spread of SARS-CoV-2, updated Nov 10 2020 to say "The prevention benefit of masking is derived from the combination of source control and personal protection for the mask wearer."

FDA - Investigational COVID-19 Convalescent Plasma: Guidance for Industry, updated November 16, 2020.

WHO - Technical specifications of personal protective equipment for COVID-19 13 November 2020.

Commentary & Press Releases

COVID-19 Infection-Preventing Clinical Deterioration. Seymour CW, Bauchner H, Golub RM. JAMA. 2020 Nov 12. doi: 10.1001/jama.2020.21720.

Challenges in Testing for SARS-CoV-2 Among Patients Who Recovered From COVID-19. Katz MH. JAMA Intern Med. 2020 Nov 12. doi: 10.1001/jamainternmed.2020.7575.

Moderna's COVID-19 Vaccine Candidate Meets its Primary Efficacy Endpoint in the First Interim Analysis of the Phase 3 COVE Study

Children and COVID-19: State-Level Data Report

Bamlanivimab for COVID-19 — Hard to Pronounce, Even Harder to Give

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