Articles about COVID-19 for May 11th to May 15th

MS Literature Review Task Force: Sherry Chao, Michael Galie, Mary Chandler Gwin, Tin Phan, Feiyun Ma, Laiken Price, Cath Rueckeis, Chris Sefton, Peter Triggiani, and Laurel Wood
Faculty Advisor: Louise King, MD

Name of Article + Link	Journal, Date	Category of Study	Question it asks	Results in Brief	Implications + Limitations
A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19	N Engl J Med. 5/7/2020	RCT (Therapeutic)	Does Lopinavir-Ritonavir (400mg/100 mg PO BID) help lower time to clinical improvement in adults with severe COVID 19? (No proven effective Tx for severe COVID 19 yet)	Open label RCT with n=199 (n=160 needed for 80% power). No placebo due to the emergency nature of the trial (trial started within days of virus). Looked at as ITT. Time to clinical improvement: 16 day vs. 16 days; hazard ratio for clinical improvement, 1.31; 95% confidence interval [CI], 0.95 to 1.85; P=0.09. No benefit in severe COVID19 compared to standard care. However, 3 pts died within 24hrs after randomization in the Lopinavir/Ritonavir group. With a modified ITT primary endpoint analysis	Authors handled and analyzed the data themselves (trial was not blinded). Authors were not able to determine the exposure of Lopinavir in this high risk pt group. Trial was 60% male. Nearly 14% of lopinavir–ritonavir recipients were unable to complete the full 1 day course of administration due to ADE (mainly GI events). "The investigators appropriately prioritized speed, designing a trial that could rapidly produce an answer. What we've learned fron their work can help inform the design of new trials. And it is clear that rapidly initiated, hig quality randomized clinical trials are possible epidemic conditions, even in the trying circumstances that prevailed in Wuhan." Thi trial began within days of the virus. Also L/R till used in some because less seriou complications (acute kidney injury and secondary infections around 1% for L/R and 5 for standard giving NNT of 25) or requiring noninvasive or invasive mechanical ventilatio for respiratory failure were fewer than in tho not receiving treatment.

				excluding those three patients showed 15d compared to 16d (hazard ratio, 1.39; 95% CI, 1.00 to 1.91) [statistically significant, but not clinically significant].	
Knowledge and Behaviors Toward COVID-19 Among US Residents During the Early Days of the Pandemic: Cross-Sectional Online Questionnaire	JMIR public health & surveillance, *medRxiv May 8 2020*	Cross-sectional online survey	How does knowledge about COVID-19 influence participation in different behaviors including self-reports of purchasing more goods than usual, attending large gatherings, and using medical masks?	Lower knowledge was associated with self-reports of engaging in purchasing more goods than necessary, attending gatherings of more than 50 people, and wearing medical masks outside the house. Differences in knowledge about COVID-19 based on age group: baby boomers in this sample were more knowledgeable about COVID-19 than all other age groups and were less likely to engage in purchasing behavior while people attending large gatherings and wearing masks in	Implications: differences in knowledge about COVID-19 appear to have prevented a coordinated effort at slowing the spread of th pandemic in the United States in the early da of the pandemic Limitations: knowledge questions were not validated, and scientific knowledge is current a moving target. This was a convenience sample of US residents from every state in th country, but people were able to self-select based on their interest and experience with the topic

				public were younger on average.	

Circulating plasma concentrations of angiotensin-converting enzyme 2 in men and women with heart failure and effects of renin–angiotensin–aldosterone inhibitors	*European Heart Journal,* May 10, 2020	Basic Science	Which factors, such as sex, disease state, etc, may be associated with increased levels of ACE2 expression? Is expression of ACE2 affected by medical RAAS blocker therapy?	Using two cohorts of CHF patients (n=2022; n=1698), plasma ACE2 levels were measured, and factors such as sex, comorbidities, and medications were assessed for association with ACE2 levels. Male sex was the strongest predictive factor for elevated plasma ACE2 (male vs female mean levels for two cohorts: 5.38 vs. 5.09 ($p<0.001$); 5.46 vs 5.16 ($p<0.001$)). No significant difference in ACE2 levels between patients with and without RAAS blockers in either cohort. One cohort showed a statistically significant difference between those on mineralocorticoid receptor antagonist therapy vs those without (5.4 vs 5.34 ($p=0.036$))	Implications: Suggests RAAS therapy does no alter plasma levels of ACE2. Limitations: This is not a population of COVID 19 patients, and therefore o direct link can be drawn. This merely feeds into our body of knowledge surrounding ACE2 expression bas on assumptions currently that the ACE2 plays some sort of role in disease infectivity and severity. Furthermore, statistically significant differences were shown, however their relati change in ACE2 levels was about 5%. It is unclear if this is clinically significant. Most importantly, authors measures plasma ACE2. The relationship between membrane bound ACE2 levels and plasma ACE2 levels is not well established, and the role of plasma ACE2 in COVID-19 pathogenesis is speculative

Characteristics of Health Care Personnel with COVID-19 — United States, February 12–April 9, 2020	CDC April 17, 2020	CDC morbidity and mortality weekly report		Between Feb 12 and Apr 9, 49,370 of the confirmed cases included a form indicating if the patient was a HCP. 9,282 (19%) were identified as HCP. Median age was 42 years and 38% reported at least one underlying health condition. 55% reported known exposure to COVID19 only in health care settings. 8% of the HCP who tested positive reported no symptoms. 90% of HCP with COVID-19 were not hospitalized; however, the 10% with more severe disease included HCP in all age groups; death was more likely in HCP aged ≥65 years.	Limitation: only 16% of confirmed cases included data on if the COVID19 patient was a HCP. Data is from forms and no statistical comparisons were performed Duration of exposure was not quantified (found another study of general practitioners in an outpatient clinic with low exposure had low risk). There may be a dosage effect. There could be an increased risk for a younger HCP compared to the general younger population.
The Disproportionate Burden of COVID-19 for Immigrants in the Bronx, New York.	*JAMA Internal Medicine*, May 8, 2020	JAMA Network Viewpoint Article	--	The Bronx is ranked the least healthy county among the 62 counties in the state of New York. Due to a disproportionate number of comorbidities, the immigrants who live in the Bronx are	The situation in the Bronx highlights the importance of targeting testing for communities who are at a higher risk of serio illness. It also highlights the need for consideration c immigrants and other populations who need accommodations while admitted to the hospital. The use of interpreters was an important example in the article. The use of

				predisposed to a greater risk of COVID-19 complications. The Bronx currently has the highest rate of COVID-19 diagnoses. Most of these immigrants already experienced a lack of access to healthcare before the pandemic and are now experiencing even higher levels of stress/lack of care.	masks and ICU equipment can make it especially hard for those who do not speak English as their first language to understand what their plan of care of is. This is especially true when family members that the patient relies on for translation are not available due to COVID-19 restrictions.
Host-viral infection maps reveal signatures of severe COVID-19 patients	May 7th, 2020, Cell	Basic Science	How does the human host interact with the virus?	Viral-Track offers an unsupervised pipeline for characterization of viral infections in scRNA-seq data by identifying infected versus bystander cells and uncovering virus-induced pathways. They identified dramatic differences between the mild and severe COVID-19 patients, including an inflammatory signature and a	Implications: potential immunotherapy treatment of severe patients by targeting the hyper inflammatory response that is activate by inflammatory cytokines such as IL-6 and IL 8. Limitations: Capture efficiency affected by properties of viral RNA molecules (presence/absence of 5' capping, poly A-tail, nucleotide composition, etc). Potential scarci of viral reads in infected cells (sampling bias)

				perturbed immune response associated with the severe manifestation of the COVID-19 disease. They also identified co-infection of SARS-CoV-2 with the human Metapneumovirus	
Coronavirus Disease-19 (COVID-19) associated with severe acute pancreatitis: Case report on three family members	*Pancreatology,* May 5, 2020	Clinical	Can acute pancreatitis arise in COVID-19 patients?	A case report of 3 family members in Denmark who contracted SARS-CoV-2 in March 2020. 2 of the 3 family members were diagnosed with acute pancreatitis associated with SARS-CoV-2 with other causes of acute pancreatitis excluded (alcohol, biliary obstruction/gall stones, drugs, trauma, hypertriglyceridemia, hypercalcemia, and hypotension). One patient. 47 y/o female, previously healthy with minimal alcohol intake and	Implications: One of the complications of COVID-19 could be acute pancreatitis, therefore pancreas-specific plasma amylase should be measured in patients with COVID-1 and abdominal pain. Acute pancreatitis can lead to multiorgan failure such as respiratory distress and kidney failure seen in both of these patients. Limitations: This is a case report with only 3 patients, and they are all related to each othe COVID-19 can result in multiorgan failure which could contribute to the pancreatitis, respiratory failure and the acute kidney disease, therefore we cannot know based on this study alone whether the acute pancreati worsened the patients' respiratory failure or kidney disease.

				negative smoking history, admitted to the ED with fever, headache, and neck pain, anorexia, sore throat and dyspnea. After admission patient developed acute kidney failure and underwent continuous veno-venous hemodialysis (CVVHD). Amylase lipase was elevated at 173 U/L upon admission and then increased to >1500 U/L after 11 hrs. Ultrasound revealed a voluminous pancreas without signs of lesions or gallstones. A Glasgow Acute Pancreatitis Score of 5 was recorded. Another patient, 68 y/o female, in this case report was admitted with epigastric pain and fever along with vomitus, diarrhea, fatigue and polydipsia. After 3	

				days of admission the patient developed acute kidney failure and CVVHD was initiated. Amylase increased from 85 U/L on the day of admission to 934 U/L and a Modified Glasgow acute pancreatitis score of 5 points. The final case in this report was a previously healthy 71 y/o man who had a low alcohol intake and no smoking history. Three days before admission the patient experienced GI symptoms with anorexia and diarrhea with a fever, dry cough and malaise. After three weeks in the ICU the patient developed increasing creatinine and oliguria and the outcome was fatal. The patient did not show signs of acute pancreatitis.	

Hypoxaemia related to COVID-19: vascular and perfusion abnormalities on dual-energy CT	Lancet Infectious Diseases 4/30/2020	Clinical	What is the underlying pathophysiology of acute hypoxic respiratory failure in COVID-19? Is it due to alveolar damage or microvascular thrombi?	Dual-energy CT was performed on three COVID-19 positive patients with severe hypoxemia, elevated D-dimer, and clinical suspicion for PE. Imaging showed striking perfusion abnormalities without evidence of PE. Pulmonary vessels were dilated proximal to and surrounding the ground-glass opacity consolidation, suggesting a failure of hypoxic vasoconstriction secondary to underlying inflammatory process that causes over-activation of vasodilation. This pathophysiology is rarely seen typical ARDS. These results suggest hypoxia in COVID-19 is due to intrapulmonary shunting secondary to endothelial dysfunction, rather than intrinsic airway disease.	It was initially believed that COVID-19 causes mortality by the typical ARDS. Recently, physicians have noticed that the hypoxia in COVID-19 does not always respond to standard treatments for ARDS, and sometime patient have high lung compliance, which is atypical for ARDS. The implication of the results that the hypoxia in COVID-19 may be explained by vascular dysfunction suggest we might need to search for other strategies outside of the standard ARDS management t target the vascular system. In addition, many new data support that COVID-19 might be more of a vascular disease due to endothelia dysfunction (eg. stroke, VTE, strong association with HTN and CVD, Kawasaki?) than a pure pulmonary process. Hopefully we will see more clinical trials targeting vascular dysfunction. The study is limited by small sample size (n= The claim of increased perfusion near the consolidation seems to be based on estimate pulmonary blood volume from the dual-energ CT image, which may not be directly correlated. It is also assumed that the area of ground glass opacification has low ventilation To accurately measure perfusion and ideally ventilation is challenging especially in patient with COVID-19. Some methods people have used to quantify perfusion and ventilation in human are multiple inert gas elimination technique and proton MRI. In addition, it is unclear how much the hypoxia issue is contributing to the mortality in COVID-19.

Humoral immune response and prolonged PCR positivity in a cohort of 1343 SARS-CoV 2 patients in the New York City region	BMJ preprint, 5 May 2020	Pub Health/Epi	What is the prevalence of SARS-CoV-2 antibodies in patients with laboratory confirmed and self-reported mild to moderate COVID-19?	1343 COVID-19 patients were recruited in NYC to assess for IgG Ab against SARS-CoV-2 using a newly FDA approved ELISA test w/ sensitivity of 92% and specificity of >99%. Of those recruited, 47% had PCR confirmed infection. Other patients were presumed COVID-19 positive based on signs and symptoms and lived with a PCR confirmed COVID-19 case, were told by a doctor they likely had COVID-19, or were a healthcare worker. At first test, 82% of PCR confirmed cases had strong Ab titer (>1:320). Of those with weak or absent Ab, 64 returned for follow up test and 57 (89%) had increased their titers to the "strong" classification. Only 4 remained weakly	Implications: Nearly all PCR confirmed patien mounted strong IgG Ab response. Given the discrepancy of Ab response between PCR confirmed and self reported cases, this suggests COVID-19 has been over diagnosed clinicians on symptoms alone. This study also gives preliminary guidelines for when Ab testing should be done (3-4 weeks after symptom onset, or at least 2 weeks after resolution). Limitations: all cases were mild, with only 3 requiring hospitalization, so results may not b generalizable to severe disease. Additionally, their analysis certainly missed asymptomatic carriers. Development of Ab protection in thi population must be studied further. The detection of Ab does not confirm immunity, but based on evidence from other corona viruses (MERS, etc) IgG has been shown to be protective in the past. All data was self reported leading to recall bias of symptom onset/resolution. Recruitment was done online and only in English. This likely skewed the study populati to young, affluent, English speakers with the ability to travel some distance to be tested at the university and missed those who were elderly, non-English speakers, and without internet access.

				positive. The 3 that were still negative self reported they had positive PCR test and no record was in the EMR. In the self reported COVID-19 group, 35% had strong titers, 3% had weak titers, 62% were negative. Neither sex nor age were associated with delayed Ab response. Median 24 days from symptom onset to strong Ab titer. Median 15 days from symptom resolution to strong Ab titer. Authors will follow cohort to assess changes in Ab over time and assess long-term immunity.	
Triple combination of interferon beta-1b, lopinavir–ritonavir, and ribavirin in the treatment of patients admitted to	The Lancet May 8,2020	Therapeutics	the efficacy and safety for triple treatment	This was a multicenter, prospective, open-label, randomized, phase 2 trial in adults with COVID-19 who were admitted to six	Limitations: This trial was open label, without a placebo group, and confounded by a subgroup withou interferon beta-1b within the combination group, depending on time from symptom ons

hospital with COVID-19: an open-label, randomised, phase 2 trial				hospitals in Hong Kong. Eligibility criteria: age>/=18y, a national early warning score 2 (NEWS2) at least 1, symptom duration </=14d. 127 patients, 86 were in the combination group and 41 were in the control group. The median age was 52 years (IQR 32–62); 68 (54%) patients were men versus 59 (46%) women. 51 (40%) patients had under-lying diseases. The median time to hospital admission from symptom onset was 5 days. The primary endpoint was the time to provide a nasopharyngeal swab negative for SARS-CoV-2 RT-PCR, the combination group had a significantly shorter median time (7 days [IQR 5–11]) than the control group (12 days [8–15]; HR 4·37 [95% CI 1·86–10·24], p=0·0010<0.05) . Combination group had a significantly	The absence of critically ill patients did not allow the generalization of these findings to severe cases. Implications: Triple antiviral therapy with interferon beta-1b lopinavir–ritonavir, and ribavirin were safe an superior to lopinavir–ritonavir alone in shortening virus shedding, alleviating symptoms, and facilitating discharge of patier with mild to moderate COVID-19 in the early stage.

				shorter time to complete alleviation of symptoms, defined as from the start of the treatment to a NEWS2 of 0, (4 days [IQR 3–8] in the combination group vs 8 days [7–9] in the control group; HR 3·92 [95% CI 1·66–9·23], p<0·0001) and SOFA score of 0 (3·0 days [1·0–8·0] vs 8·0 days [6·5–9·0]; HR 1·89 [1·03–3·49], p=0·041; table 2). There was a shorter median hospital stay in the combination group than in the control group (9·0 days [7·0–13·0] vs 14·5 days [9·3–16·0]; HR 2·72 [1·2–6·13],p=0·016). For the virological outcome, the nasopharyngeal swab viral load was significantly lower in the combination group than in the control group from day 1 to day 7 after treatment. Similar results were found in the posterior oropharyngeal saliva, throat swab, and stool specimens after treatment.	

				The most common adverse events were diarrhoea (52 [41%] of 127 patients), fever (48 [38%] patients), nausea (43 [34%]) and raised alanine transaminase level (18[14%]).These side effects mostly resolved within 3 days after drug initiation. There were no differences between incidence of any of the adverse events or durations of nausea or diarrhoea between the treatment groups. One patient in the control group had a serious adverse event of impaired hepatic enzymes requiring discontinuation of treatment.	
Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19	New England Journal of Medicine May 7, 2020	Observational study (Therapeutics)	Does hydroxychloroquine (600 mg BID x1d then 400 mg daily x4d) reduce patients requiring intubations or reduce mortality in patients with COVID19 compared	This observational study was a single center (NY) and had n=1446. In a crude, unadjusted analysis, patients who had received hydroxychloroquine were more likelyto	Pts on sarilumab or remdesivir may have skewed data. The Tx of hydroxychloroquine was non randomized (however they tried to adjust this by also adding data for propensity score). About 65% of the patients were Hispanic. Hydroxychloroquine groups had almost 2-3x more pts at baseline exposed to glucocorticoids compared to non hydroxychloroquine groups.

			to patients not receiving hydroxychloroquine?	have had a primary end-point event than were patients who did not (hazard ratio, 2.37; 95% CI, 1.84 to 3.02). In analysis according to the propensity score, there was no significant association between hydroxychloroquine use and the composite primary endpoint (hazard ratio, 1.04; 95% CI, 0.82 to 1.32)	Hydroxychloroquine also had more pts on azithromycin, other abx, or tocilizumab compared to non hydroxychloroquine pts. More non Tx pts had a higher PaO2:FiO2 ratio (more is generally better but not always connected to event outcomes). The propensity score analysis is significant on COVID Tx current procedures. Preliminary da from small, low powered, not well-adjusted studies showed some benefit to hydroxychloroquine. With this more reliable data it is shown that this drug is not significan in reducing mortality or intubations. This is a good thing, because when certain politicians started talking about this drug it went on shortage. Pharmacists (source from persona chats) have told me that they had to start holding onto this drug and refusing it for som indications (like COVID) because pts with a significant need for it (such as arthritis pts) were not able to get the Tx they needed. There have also been a few prescribers caugh writing this medication for family members prophylactically adding to the shortage (this got so bad that legislation was passed taking away the ability for dentists to prescribe this drug in Australia). Until RCT show otherwise, hopefully this trial will allow for normal stock of hydroxychloroquine to those who have evidence based benefit for it.
Race, Socioeconomic Deprivation, and Hospitalization for	*MedRxiv* May 2nd, 2020	Prospective cohort study (UK Biobank 500 000) but used	What is the extent to which disparities in health outcomes between white and	Both black participants (odds ratio 3.4; 95%CI 2.4–4.9) and Asian	Implications: higher morbidity in non-white individuals in the context of a large populatio of participants in a national biobank. Need further study to investigate whether risk is

COVID-19 in English participants of a National Biobank		as case-control for COVID-19 (?)	non-white minorities related to socioeconomic versus biologic factors?	participants (odds ratio 2.1; 95%CI 1.5−3.2) were at substantially increased risk as compared to white participants. We further observed a striking gradient in COVID−19 hospitalization rates according to the Townsend Deprivation Index − a composite measure of socioeconomic deprivation − and household income. Adjusting for such factors led to only modest attenuation of the increased risk in black participants, adjusted odds ratio 3.1 (95%CI 2.0−4.8)	related to previous comorbidities. With respe to potential biologic factors, ongoing efforts seek to determine whether genetics--known both vary substantially across racial groups a contribute to pre-existing comorbidities--play an important role in COVID-19 disease severi Limitations: First, the UK Biobank enrolled individuals on a volunteer basis and is not a population-based study--additional efforts ar needed to generalize these observations in other settings. Second, Townsend Deprivatio Index and household income were assessed a enrollment, and participants' status may hav changed in subsequent years. Third, addition and more sophisticated analytic techniques may prove useful in further disentangling COVID-19 related disparities.
School Closure and Management Practices During Coronavirus Outbreaks Including COVID-19: A Rapid Systematic Review	The Lancet Child & Adolescent Health May 2020,	Epidemiology: Systematic Review.	"what is known about the use of and effectiveness and cost-effectiveness of school closure and other school social distancing practices on infection rates and transmission during coronavirus outbreaks?"	16 published studies from the 2003 SARS outbreak were included in this review. All social distancing measures combined during COVID-19 have decreased transmission by up to 44%. This is much greater than the estimated 10–15% reduction in influenza transmission from school closures alone during the	Interactions between children and adults and between children at different schools increases during holidays and school closures, which may limit the effectiveness of school closures. These studies do not account for the potential confounder o parents having to work from home to teach their children. Closures of schools may impact our healthcare workforce as is estimated 29% of health-care workers have childcare obligations. This study suggest the ongoing need to provide resources to our healthcare workers with their family obligations.

				2009 pandemic in Hong Kong. One study found that "school closures made very little difference to the prevention of SARS in Beijing, given the very low attack rate in schools before the closure and the low prevalence in children." However, the prevalence of COVID19 in children is not fully understood. One study of the Beijing SARS outbreak found "school closures occurred after the R had dropped below 1 and that school closures in this case added little to control of the outbreak." During the SARS outbreak in China there were specific class cancellation policies, but college students remained on campus. There was no recorded transmission of SARS in schools during the outbreak in China at that time. One study used viral surveillance during a 5-day closure of nearly all schools in the greater Seattle metropolitan area in February, 2019. This closure occurred due increases in these viruses believed due to extreme weather. Their study estimated "school	There is very little guidance available to schools for how to remain open with alternative social distancing practices. On review from 2018 only included a few cases of schools that increased spacing between students during transport and in class, and cancelled school activities that required large student mixing, but no data was found on any detailed polic There is no data on child to child transimission of covid19 "One study from the UK Department of Health in 2014, to inform influenza pandemic preparations, included 100 epidemiological and 45 modelling studies and concluded tha school closures are likely to have the greatest effect if the virus has low transmissibility and if attack rates are higher in children than in adults." A 2015 systematic review of social of school closures for influenza pandemics reported a wide variation in the reduct of transmission (range 1–50%); however, up to 70% of students shifted social contacts to other sites during closure

				closures resulted in a 5·6% (95% CI 4·1–6·9) reduction in coronavirus infections, similar to influenza H1N1 (7·6%; 5·2–9·7) but higher than influenza H3N2 (3·1%; 2·5–3·2), all of which were prevalent at the time." In a non- peer-reviewed report from Ferguson and colleagues31 modelled the estimated effects of a range of different social distancing measures and combinations of measures. They predict school closure alone may reduce total COVID19 Deaths by around 2–4% in the UK, whereas other single measures such as case isolation would be more effective, and a combination of other measures would be the most effective.	

COVID-19: How to Recognize and Manage Kawasaki-like Syndrome	Medscape News Article May 8, 2020	Clinical/ Epidemiological	What do we know about the increase of cases of an inflammatory syndrome very similar to Kawasaki disease?	This article is from a pediatric cardiologist in France who discusses the 20 or so cases she has seen in the PICU of a syndrome very similar to Kawasaki disease but not quite "classic Kawasaki." He reports a large variability in presentation; however, most are associated with circulatory failure and myocarditis. There is usually an increase in Kawasaki cases during the winter and spring, but during the COVID19 epidemic this multisystem inflammatory Kawasaki-like syndrome have risen in an "epidemic nature." The ICUs in Île-de-France (the region around Paris) saw 25 cases in 3 weeks. There were 9 cases at Necker hospital over the past 2 days (as of April 30). "our British, Spanish, Italian, and Belgian colleagues confirm this as an emerging problem." Patients in France were initially described	Physicians should take care to document the clinical presentation of those with COVID19 and cardiac/vascular complications to collect more da on this inflammatory syndrome affect the vasculature.

				as having a respiratory, hemodynamic, septic, or digestive presentation. Cardiac collapse is common +/- LV systolic dysfunction. The treatment is the exact same as for Kawasaki (aspirin+IVIG) and patients typically respond well to treatment.	

Characteristics and Clinical Outcomes of Adult Patients Hospitalized with COVID-19 – Georgia, March 2020	CDC Morbidity and Mortality Weekly Report (MMWR), May 8, 2020		What are the characteristics of adult patients hospitalized in metropolitan Atlanta and Southern Georgia?	Data was abstracted for laboratory confirmed COVID-19 patients hospitalized from March 1 – 30, 2020 from 8 hospitals in Georgia: 7 Atlanta Metropolitan hospitals (5 community, 1 university and 1 public hospital) and 1 community hospital in Southern Georgia. There were 305 patients, and 50.5% of them were female, 284 (93%) hospitalized in the Metropolitan Atlanta hospitals. 297 (93%) had race and ethnicity data which was categorized as black non-Hispanic (247, 83.2%) and nonblack patients (50, 16.8%). The median age of admission was not significantly different between black and nonblack patients. These two groups	Implications: Public Health efforts (preventio activities, etc) should be geared towards/prioritized for communities that are being disproportionately affected. Additional it was suggested that serious illness can occu among all adults, regardless of underlying conditions or age, therefore all adults should be educated on the risk of severe illness and the appropriate measures to take to decreas the chance of infection. Additional research needs to be conducted to understand why some populations are being disproportionate represented in hospitalized patients – especially investigating, factors such as social economic, occupational, environmental, etc etc. Limitations: The authors mention that the da was collected in a convenient manner to quickly generate results. The patients were n tracked following discharge, therefore their morbidity or mortality after hospitalization is unknown. Lastly, race and ethnicity data was abstracted from medical records, and each system has a different way of recording this data, which could result in misclassification.

				had similar probability of receiving IMV or death during hospitalization. The proportion of hospitalized patients who were black was higher than expected based on overall hospitalization. At four affiliated hospitals which had 67% of the patients in this cohort, 80% of the patients were black compared to the 47% of patients hospitalized overall during March. And while a larger proportion of older patients had worse outcomes, there was still a considerable proportion fo patients aged 18-64 y/o without high-risk conditions that received ICU-level care and died.	

Structural Basis for the inhibition of SARs-CoV-2 main protease by antineoplastic drug carmofur	*Nature*, May 07, 2020	Basic Science	How does carmofur inhibit the main protease of SARS-CoV-2?	This study was performed because we knew that carmofur inhibited the main protease of SARS-CoV-2, but the mechanism of this process was unknown. It was shown that carmofur in complex with the main protease modifies the catalytic Cys145 of the main protease.	Implications: This main protease is highly conserved among all coronaviruses. This cou serve as a target for treatment, or possibly assist with prevention planning (I.e. a vaccine Given the initial success of hydroxychloroquin + azithromycin. It's important to continue to explore other options in case the current trip drug therapy plan is not as successful as we hope it will be. Limitations: This study was performed in a ce line, so the results cannot be extrapolated to determine the efficacy of the treatment of COVID-19 with carmofur in the body.
Hyperinflammatory shock in children during COVID-19 pandemic	*The Lancet,* May 7, 2020	Retroactive case report of 8 children in SE England	How did children with COVID-19 and a Kawasaki-like inflammatory disease present?	Data was reviewed from a cluster of 8 children presenting with hyperinflammatory shock within a period of 10 days in mid April. Normal prevalence is 1-2 children per week. Clinical features of this disease presented similar to atypical Kawasaki disease, Kawasaki disease shock	All children tested negative for SARS-CoV-2 o BAL or nasopharyngeal aspirates. No pathological organism was IDed in 7 children. Adenovirus and enterovirus isolated in 1 chil C-reactive protein, procalcitonin, ferritin, triglycerides and D-dimers were all positive. Treatment included IV Ig (2g/kg q1 first day), ceftriaxone, clindamycin, and 50 mg/kg aspir All were discharged from PICU 4-6 days. 2 tested positive for SARS-CoV-2. ECGs were non specific, echo-bright coronary vessels were found in all patients. 1 patient passed do to progression to giant coronary aneurysm, arrythmia, ECMO, and cerebrovascular infarct, after discharge.

				syndrome or toxic shock syndrome. All children were well, 5 males 3 females, except one was well above 75 percentile for weight. 4 had known family exposure to coronavirus disease 2019. Ages ranged from 4-14 years. Symptoms included unrelenting fever, variable rash, conjunctivitis, peripheral edema, and extremity pain with significant gastrointestinal symptoms. All progressed to warm, vasoplegic shock which was refractory to volume resuscitation; they eventually needed noradrenaline and milrinone. NO respiratory symptoms noted, although 7 needed mechanical	20 more children presented similarly 1 week after submission of the article, the first 10 of whom tested positive for SARS-CoV-2. Sugges previously asymptomatic children with SARS-CoV-2 infection can manifest as hyperinflammatory syndrome with multiorga involvement. Good reading for the clinician: https://discoveries.childrenshospital.org/cov 19-inflammatory-syndrome-children/

				ventilation for cardiac stabilization. Some generalized effusions (pleural, pericardial and ascitic), suggesting diffuse inflammatory process.	
Risk Factors for Mortality in 244 Older Adults With COVID-19 in Wuhan, China: A Retrospective Study	May 8th, 2020 Journal of American Geriatrics Society	Retrospective case-control	What are potential risk factors for mortality in older patients with coronavirus on admission, which may help identify those with poor prognosis at an early stage?	**In short**: Older age and lower LYM count on admission were associated with death in hospitalized COVID-19 patients. **Details:** Univariate analysis revealed that several clinical characteristics and laboratory variables were significantly different (ie, *P* < .05) between discharged and deceased patients. Multivariable logistic regression analysis revealed that lymphocyte (LYM) count (odds ratio [OR] = 0.009; 95% confidence interval [CI] = 0.001-0.138; *P* = .001) and older age (OR = 1.122; 95% CI = 1.007-1.249; *P* =	**Implications:** immunosenescence is a major cause of mortality. (common in pneumonia o other bacterial/viral/fungal causes, too) **Limitations**: retrospective study therefore more than one-third of patients did not have laboratory data for IL-6 and serum ferritin levels (their roles may have been under-estimated in predicting death during hospitalization). The study did not include treatments such as antiviral and glucocorticoid therapy. Third, this was a single-center study from the Sino-French New City Branch Tongji Hospital, which mainly admitted severe cases of COVID-19; as such, the results may be biased.

				.037) were independently associated with hospital mortality. White blood cell count was also an important risk factor (*P* = .052). The area under the receiver operating characteristic curve in the logistic regression model was 0.913. Risk factors for in-hospital death were similar between older men and women.	

A noncompeting pair of human neutralizing antibodies block COVID-19 virus binding to its receptor ACE2	*Science,* 13 May 2020	Basic Science	Are the antibodies isolated from a patient with COVID-19 specific for SARS-CoV-2? Do they have neutralizing ability?	The researches isolated specific single memory B-cells from COVID-19 patient peripheral blood mononuclear cells (PBMCs). They amplified the variable regions for the heavy and light chains and cloned into a vector with constant region to produce IgG1 antibodies. The plasmids were co-transferred into HEK 293T cells with paired heavy and light chains. The supernatants were screened for binding to the RBD by bio-layer interferometry. There were supernatants from 4 different antibodies (B5, B38, H2 and H4) that bound to COVID-19 virus RBD but not to SARS-CoV-RBD suggesting the epitopes are immunologically different.	Implications: This molecular information for epitopes on COVID-19 RBD could help with developing a vaccine. Additionally, understanding the neutralizing antibody features could help in developing a synthetic therapeutic or the utilization of antibodies as prophylactic or therapeutic treatment. Limitations: This paper details the binding properties of two isolated antibodies from a single COVID-19 patient. It would be interesting to see the similarities/differences antibodies isolated from more patients with COVID-19. And while the *in vivo* studies showed a reduction in virus titer, which validated the results from the cell culture experiments, additional studies are required determine the titer of antibody required to have a therapeutic benefit and whether the timing of antibody administration alters clinic outcomes.

				All of these antibodies exhibited neutralizing ability even in the presence of a higher titer of SARS-CoV-2 virus. They performed a competition assay that showed B38 and H4 have complete competition with ACE2 for binding to RBD. B5 showed partial competition and H2 did not compete with ACE2 for RBD. By performing an epitope competition assay, it was suggested that B38 and H4 recognizes different epitopes with partial overlap. hACE2 transgenic mice were administered a single dose of B38 or H4 12 hours after a COVID-19 viral challenge. The body weight of B38 group decreased slowly and recovered at 3 days post infection compared	

				with the PBS control group and H4 group. The RNA copies of both B38 and H4 were significantly lower than PBS group with a 32.8% and 26% reduction respectively. Histopathological examination indicated that severe bronchopneumonia and interstitial pneumonia can be observed in mice of PBS group. Mild bronchopneumonia was observed in the H4 group and no lesions observed in the B38 group. Complex crystal structure of RBD-B38 and RBD-H4 complexes were obtained. The three Complementarity Determining Regions (CDRs) on the heavy chain and two CDRs on the light chain are involved in the interaction with RBD. There are 36	

				residues in the epitope that interact with B38, with most contacts being hydrophilic interactions, which they believe to explain the difference in B38 binding between COVID-19 rather than SARS-CoV. Complex structures of RBD/B38-Fab and RBD/hACE2 were superimposed and both the Vh and VL of B38 would sterically hinder ACE2 binding. The RBD in B38 bound form and hACE2-boudn form have not significant conformational changes. 18 of the 21 amino acids on the RBD are involved in binding both B38 and ACE2, which might explain why B38 abolishes the binding between COVID-19 virus RBD and the receptor.	

Characteristics and Outcomes of Recipients of Heart Transplant with Coronavirus Disease 2019	*JAMA Cardiology*, May 13, 2020	Clinical; single-center case series	What are the characteristics and outcomes of COVID-19 infections in heart transplant recipients?	Preliminary case reports have not indicated a higher incidence of infections within the posttransplant population. 28 heart transplant recipients were identified over a six-week period that had a laboratory confirmed diagnosis of COVID-19. The median age of the patients was 64.0 (IQR 53.5-70.5) years. 22 (79%) of the patients were men. The median time from heart transplant was 8.6 (IQR, 4.2-14.5) years. Comorbid conditions included hypertension, diabetes, and cardiac allograft vasculopathy. Twenty-two participants (79%) were admitted for treatment, and 7 (25%) required mechanical	Implications: The question this study set out t answer is important because it helps to furth characterize the disease course in immunosuppressed individuals. It was previously thought that immunosuppression helped to prevent cytokine storm. It is also important to further characterize cardiac involvement of the disease. This article also studied management of transplant patients with coronavirus 2019 infection and recommended these patients b managed in a transplant center. Limitations: The authors state there were issues with testing milder/asymptomatic case so they may have underestimated the prevalence of COVID-19 in the transplant population. They were also unable to determine if cardiovascular risk factors, immunosuppression or heart transplant statu increased the risk of mortality.

				ventilation. Most had evidence of myocardial injury measured by high-sensitivity Troponin T and elevated inflammatory biomarkers (CRP, IL-6). Among patients managed at the study institution, mycophenolate mofetil was discontinued in most patients and a small number of the patients had a reduction in the dose of their calcineurin inhibitor. Treatment of COVID-19 included hydroxychloroquine (18 patients [78%]), high-dose corticosteroids (8 patients [47%]), and interleukin 6 receptor antagonists (6 patients [26%]). Overall, 7 patients (25%) died. Among 22 patients (79%) who were admitted,	

				11 (50%) were discharged home, 4 (18%) remain hospitalized at the end of the study, and 7 (32%) died during hospitalization.	

An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study	*The Lancet* May 13, 2020	Epidemiological observational cohort study of Kawasaki-like disease cases in Italy for the past 5 years	What is the change in incidence and presentation of Kawasaki-like diseases in the past month?	The city of Bergamo has the highest rate of infections and deaths by SARS-CoV-2 in Italy. The notes of patients diagnosed with Kawasaki disease admitted to the General Paediatric Unit of Hospital Papa Giovanni XXIII (largest PICU volume in N. Italy), for the last 5 years up to April 20, 2020 were reviewed. Kawasaki-like presentations were divided into 2 types: classic (fever 5+ days + 4 clinical criteria) and incomplete (fever 5+ days + 2-3 clinical criteria). Various criteria also defined Kawasaki Disease Shock Syndrome and Macrophage Activation Syndrome. Post February 17 (local epidemic start	The increased incidence points to a link between COVID-19 and Kawasaki-like disease In addition, Kawasaki disease incidence has been historically higher (Japan studies) in winter months, unlike these April presentations. A 2005 study also found a nov human coronavirus (New Haven coronavirus HCoV-NH) in respiratory secretions of 8/11 Kawasaki affected children vs 1/22 controls b RT-PCR. A retrospective study in Japan found contrarily 0/19 Kawasaki affected children vs 5/208 controls by RT-PCR. This could be a secondary morbidity of COVID 19. This disease might present outside classic Kawasaki. This disease also presents more severely (resistance to IV Ig, needing adjuncti steroids, developing KDSS and MAS), requirin more prompt and aggressive management. This disease may also present late, as suggested by the IgG positive serology. Serology may be more reliable than RT-PCR i determining cause of infection. More researc is needed on immune response to viral triggers. Still remains rare, estimated to affec no more than 1/1000 children exposed to SARS-CoV-2.

				date), 10 patients presented with Kawasaki-like disease: 50% classic, 50% incomplete. Chest X-ray was positive in 50% for minimal mono or bilateral infiltrates. Cardiac issues were present in 40%, 2 needing inotropic support. KDSS, MAS or both were present in 70%. Nasopharyngeal and oropharyngeal swab RT-PCR for SARS-CoV-2 was positive in 20%. Serology for SARS-CoV-2 was IgG positive in 80%, IgM positive in 30%. All discharged. This marks a $p<0.00001$ statistically significant 30-fold increase in Kawasaki-like disease incidence (0.019% --> 3.5%), controlled for geographical catchment variations. From	

				January 1 2015 to February 17 2020, the hospital only had 19 cases total. In addition, none of these pre-epidemic patients developed MAS or KDSSS ($p<0.021$). Only 31% of these patients presented incomplete ($p<0.43$).	
Vitamin D Supplementation Could Possibly Improve Clinical Outcomes of Patients Infected with Coronavirus-2019 (COVID-19)	SSRN May 7, 2020	Clinical: retrospective multicenter	Is vitamin D status associated with COVID-19 outcome?	A retrospective multicentre study of 212 cases from three hospitals in Southern Asian countries with confirmed COVID-19 was done to investigate the association between serum 25(OH)D level and clinical outcomes. Serum 25(OH)D levels were lowest in the critical cases and highest in the mild cases (17.1 vs 31.2 ng/mL, $p<0.001$). Severe cases also had higher proportion of vitamin D deficiency compared to mild cases (31% vs 1.4%, $p<0.001$). For each standard deviation increase in serum 25(OH)D, the odds of having a mild clinical	Implication: Serum vitamin D status may account for the broad spectrum of COVID-19 disease outcome. Supplementing vitamin D to hospitalize COVID-19 patients may be a cost-effective metho to improve outcomes, especially in patients with vitamin D deficiency. Limitation: The cases are reported to come from hospitals in Southern Asian, but unclear which countries the cases are from. The population studied might have higher prevalence of vitamin deficiency compared to the US (eg. due to skin pigmentation). The prevalence of vitamin D deficiency in this study is 36%. However, a quick search for vitamin D status in the US population revealed 40% of population with vitamin D deficiency. In addition, African American population has a much higher prevalence of vitamin D deficiency (odds ratio=3), which might partly explain the differential disease outcome in COVID-19. RCT is needed to address confounding (eg. poor nutrition correlates with poor health), although a previous RCT showed vitamin D supplement reduces risk of upper respiratory infection, which is promising.

				outcome rather than a critical outcome were increased approximately 19.61 times (OR=0.051, p<0.001).	
Hyperbaric oxygen therapy in preventing mechanical ventilation in COVID-19 patients: a retrospective case series	*Journal of Wound Care,* May 2020 PRE-PRINT	Clinical/Therapeutic	Can hyperbaric oxygen therapy improve oxygen saturation in patients with COVID-19?	In this retrospective case series, 5 patients were given hyperbaric oxygen therapy (HBOT) instead of mechanical ventilation. A decrease in oxygen requirement below an FiO2 of 50% took an average of 5 treatment sessions. All patients recovered (increased oxygen saturation, tachypnoea improved, and inflammatory markers decreased) without requiring mechanical ventilation.	Implications: There is the possibility that HBO can be used instead of mechanical ventilation for some patients. Limitations: This is a small study (n = 5), so further studies would have to be done. Additionally, the authors mention that the patients were predominately female in this study, which is not consistent with previous reports of hospitalized patients.
Review article: COVID-19 and liver disease - what we know on 1st May 2020		Clinical Systematic Review	What are the changes in LFTs in patients with COVID19 and is there any relationship between chronic	COVID-19 is frequently associated with abnormal LFTs, particularly mildly elevated transaminases. Clinically significant	It is unknown if this is due to the virus itself or the various drugs used in treatment. Children with COVID19 do not typically have increased LFTs, thu a child with increased LFTs warrants further workup.

			liver disease and COVID19?	liver impairment is rare. Patients with chronic liver disease do not appear to be at increased risk of contracting COVID19; however, those with cirrhosis, hepatocellular carcinoma, non-alcoholic fatty liver disease, autoimmune liver diseases or liver transplant may have a greater risk for severe COVID-19.	

Youtube: COVID-19 Literature Updates: Part 4 (Richterman & Meyerowitz)

Name of article	Journal/Date	Summary
CORIMUNO-19 Tocilizumab trial	Press release. April 28, 2020	The primary composite outcome was need for ventilation (non-invasive or mechanical) or death at day 14. Preliminary result: A total of 129 patients were randomized: 65 to standard of care + tocilizumab and 64 to standard of care alone. A significantly lower proportion of patients reached the primary outcome in the tocilizumab arm.
Detection of SARS-CoV-2 in Different Types of Clinical Specimens	JAMA March 11, 2020	The virus can be detected in various specimens: Bronchoalveolar lavage fluid specimens showed the highest positive rates (93%), followed by sputum (72%), nasal swabs (63%), fibrobronchoscope brush biopsy (46%), pharyngeal swabs (32%), feces (29%), and blood (1%). No urine was positive.
High frequency of SARS-CoV-2 RNAemia and association with severe disease	medRxiv May 1, 2020	RNAemia was detected more frequently in individuals who developed severe disease including the need for ICU transfer (32.1% vs 14.0%; p=0.05), mechanical ventilation (21.4% vs 3.5%; p=0.01) and 30-day all-cause mortality (14.3% vs 0%; p=0.01).

SARS-CoV-2 productively infects human gut enterocytes	Science May, 1. 2020	ACE2 is highly expressed on enterocytes, and intestinal epithelium supports SARS-CoV-2 replication, demonstrated in human small intestinal organoids as model system.
Second-Trimester Miscarriage in a Pregnant Woman With SARS-CoV-2 Infection	JAMA, April 30, 2020	Case report on a pregnant woman with second trimester (19w) miscarriage as the clinical manifestation of COVID-19, with evidence of placental infection.
Presence of SARS-CoV-2 reactive T cells in COVID-19 patients and healthy donors	medRxiv April 17, 2020	Common cold shares higher similarity with COVID-19 in the C terminal of S protein. Authors found COVID-19 patients S-reactive CD4+ T cells equally targeted both N-terminal and C-terminal parts of S whereas in healthy donors S-reactive CD4+ T cells reacted almost exclusively to the C-terminal, suggesting adaptive immune response partially explains the broad spectrum of illness severity.
Hypoxemia related to COVID-19: vascular and perfusion abnormalities on dual-energy CT	Lancet Infectious Diseases. April 30, 2020	Case study on 3 patients with severe hypoxemia and elevated D-dimer. Dual-energy CT showed striking perfusion abnormalities without PE. Results suggests hypoxia is due to intrapulmonary shunting due to failure of hypoxic vasoconstriction secondary to underlying inflammatory process, rather than intrinsic airway disease.
Early Self-Proning in Awake, Non-intubated Patients emergency Department: A Single ED's Experience during the COVID-19 pandemic	SAME April 22. 2020	In 50 patients in an NYC ED, SpO2 improves from 80% on arrival to 94% after 5 minutes of proning.
Pulmonary Embolism in COVID-19 Patients: Awareness of an Increased Prevalence	Circulation April 24, 2020	Among 107 COVID-19 patients in French ICU, 20.6% had PE, significantly higher than control's 6.1%
COVID-19 and its implications for thrombosis and anticoagulation	Blood, April 27, 2020	The authors suggested COVID-19 associated coagulopathy should be managed as it would be for any critically ill patient, following the established practice of using thromboembolic prophylaxis for critically ill hospitalized patients. Current data do not suggest the use of full intensity anticoagulation doses unless otherwise clinically indicated.