

COVID-19 Resource Desk

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Retraction Watch

New Research

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COVID-19 related publications by Providence caregivers – see Digital Commons

Clinical Syndrome

 Prevalence and Predictors of Venous Thromboembolism or Mortality in Hospitalized COVID-19 Patients. Cohen SL, Gianos E, Barish MA, et al. *Thromb Haemost.* 2021 Jan 20. doi: 10.1055/a-1366-9656. <u>https://www.thieme-</u>

connect.de/products/ejournals/abstract/10.1055/a-1366-9656

Findings: A retrospective cohort study of adult COVID-19 patients admitted to an integrated health care network in the New York metropolitan region between March 1, 2020 and April 27, 2020. The final analysis included 9407 patients with an overall VTE rate of 2.9% (2.4% in the medical ward and 4.9% in the ICU) and a VTE or mortality rate of 26.1%. Most patients received prophylactic-dose thromboprophylaxis. Multivariable analysis showed significantly reduced VTE or mortality with Black race, history of hypertension, angiotensin converting enzyme/angiotensin receptor blockers use, and initial prophylactic anticoagulation. It also showed significantly increased VTE or mortality with age 60 years or greater, Charlson Comorbidity Index (CCI) of 3 or greater, patients on Medicare, history of heart failure, history of cerebrovascular disease, body mass index greater than 35, steroid use, anti-rheumatologic medication use, hydroxychloroquine use, maximum D-dimer 4 times or greater than the upper limit of normal (ULN), ICU level of care, increasing creatinine, and decreasing platelet counts. CONCLUSION: In our large cohort of hospitalized COVID-19 patients, the overall in-hospital VTE rate was 2.9% (4.9% in the ICU) and a VTE or mortality rate of 26.1%. Key predictors of VTE or mortality included advanced age, increasing CCI, history of cardiovascular disease, ICU level of care, and elevated maximum D-dimer with a cutoff at least 4 times the ULN. Use of prophylactic-dose anticoagulation but not treatment-dose anticoagulation was associated with reduced VTE or mortality.

 Prevalence of Thrombotic Complications in ICU-Treated Patients with Coronavirus Disease 2019 Detected with Systematic CT Scanning. Mirsadraee S, Gorog DA, Mahon CF, et al. *Crit Care Med.* 2021 Jan 6. doi: 10.1097/CCM.00000000004890. <u>https://journals.lww.com/ccmjournal/Abstract/9000/Prevalence of Thrombotic Complication</u> <u>s in.95395.aspx</u> Findings: There is a high prevalence of thrombotic complications, mainly pulmonary, among coronavirus disease 2019 patients admitted to ICU, despite anticoagulation. Detection of thrombus was usually incidental, not predicted by coagulation or inflammatory biomarkers, and associated with increased risk of death. Systematic CT imaging at admission should be considered in all coronavirus disease 2019 patients requiring ICU.

- 3. Clinical presentation and mortality in hospitalized patients aged 80+ years with COVID-19-A retrospective cohort study. Karlsson LK, Jakobsen LH, Hollensberg L, et al. Arch Gerontol Geriatr. 2020 Dec 30;94:104335. doi: 10.1016/j.archger.2020.104335. https://www.sciencedirect.com/science/article/pii/S0167494320303319 Findings: This retrospective study included patients ≥80 years of age with a positive test for SARS-CoV-2, who were admitted to one of three medical departments in Denmark from March 1st to June 1st, 2020. A total of 102 patients (47% male) with a mean age of 85 years were included. The most common symptoms at admission were fever (74%), cough (62%), and shortness of breath (54%). Furthermore, atypical symptoms like confusion (29%), difficulty walking (13%), and falls (8%) were also present. In-hospital and 30-day mortality were 31% (n = 32) and 41% (n = 42), respectively. Mortality was highest in patients with confusion (50% vs 38%) or falls (63% vs 39%), and nursing home residency prior to hospital admission was associated with higher mortality (OR 2.7, 95% CI 1.1-6.7). Older patients with SARS-Cov-2 displayed classical symptoms of COVID-19 but also geriatric frailty symptoms such as confusion and walking impairments. Additionally, both in-hospital and 30-day mortality was very high. Our study highlights the need for preventive efforts to keep older people from getting COVID-19 and increased awareness of frailty among those with COVID-19.
- The clinical spectrum of COVID-19-associated cutaneous manifestations: an Italian multicentre study of 200 adult patients. Marzano AV, Genovese G, Moltrasio C, et al. J Am Acad Dermatol. 2021 Jan 18:S0190-9622(21)00166-3. doi: 10.1016/j.jaad.2021.01.023. https://www.jaad.org/article/S0190-9622(21)00166-3/fulltext

Findings: Twenty-one Italian Dermatology Units were asked to collect the demographic, clinical and histopathological data of 200 patients with COVID-19-associated skin manifestations. A chilblain-like acral pattern significantly associated with a younger age (p<0.0001) and, after adjusting for age, significantly associated with less severe COVID-19 (p=0.0009). However, the median duration of chilblain-like lesions was significantly longer than that of the other cutaneous manifestations taken together (p<0.0001). Patients with moderate/severe COVID-19 were more represented than those with asymptomatic/mild COVID-19 among the patients with cutaneous manifestations other than chilblain-like lesions, but only the confluent erythematous/maculo-papular/morbilliform phenotype significantly associated with more severe COVID-19 (p=0.015), and this significance disappeared after adjusting for age. After adjusting for age, there was no clear-cut spectrum of COVID-19 severity in patients with COVID-19-related skin manifestations although chilblain-like acral lesions were more frequent in younger patients with asymptomatic/Paucisymptomatic COVID-19.

5. Risks of AKI and Major Adverse Clinical Outcomes in Patients with Severe Acute Respiratory Syndrome or Coronavirus Disease 2019. Teoh JY, Yip TC, Lui GC, et al. J Am Soc Nephrol. 2021

Jan 22:ASN.2020071097. doi: 10.1681/ASN.2020071097. https://jasn.asnjournals.org/content/early/2021/01/21/ASN.2020071097

Findings: We identified 1670 patients with SARS and 1040 patients with COVID-19 (median ages, 41 versus 35 years, respectively). Among patients with SARS, 26% met the primary endpoint versus 5.3% of those with COVID-19. Diabetes mellitus, abnormal liver function, and AKI were factors significantly associated with the primary endpoint among patients with either SARS or COVID-19. Among patients with SARS, 7.9%, 2.1%, and 3.7% developed stage 1, stage 2, and stage 3 AKI, respectively; among those with COVID-19, 6.6%, 0.4%, and 1.1% developed stage 1, stage 2, and stage 3 AKI, respectively. In both groups, factors significantly associated with AKI included diabetes mellitus and hypertension. Among patients with SARS. Renal function recovery usually occurred within 30 days after an initial AKI event. AKI rates were higher among patients with SARS than those with COVID-19. AKI was associated with major adverse clinical outcomes for both diseases. Patients with diabetes mellitus and abnormal liver function were also at risk of developing severe consequences after SARS and COVID-19 infection.

 Occurrence of Invasive Pulmonary Fungal Infections in Severe COVID-19 Patients Admitted to the ICU. Fekkar A, Lampros A, Mayaux J, et al. *Am J Respir Crit Care Med.* 2020 Dec 2. doi: 10.1164/rccm.202009-3400OC. <u>https://www.atsjournals.org/doi/pdf/10.1164/rccm.202009-34000C</u>

Findings: Our study population included a total of 145 patients the median age was 55 years old, most of them were male (n=104; 72%), were overweight (n=99; 68%), suffered from hypertension (n=83; 57%) and diabetes (n=46; 32%). Few patients presented preexisting host risk factors for invasive fungal infection (n=20; 14%). Mycological analysis included 2815 mycological tests (culture, galactomannan, beta-glucan, PCR) performed on 475 respiratory samples and 532 sera. A probable/putative invasive pulmonary mold infection was diagnosed in 7 (4.8%) patients and linked to high mortality. In patients with no underlying immunosuppression, severe SARS-CoV-2 related pneumonia seems at low risk of invasive fungal secondary infection, especially aspergillosis.

7. **Microthrombi as a Major Cause of Cardiac Injury in COVID-19: A Pathologic Study.** Pellegrini D, Kawakami R, Guagliumi G, et al. *Circulation*. 2021 Jan 22. doi:

10.1161/CIRCULATIONAHA.120.051828.

https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.051828

Findings: Of the 40 hearts examined, 14 (35%) had evidence of myocyte necrosis, predominantly of the left ventricle. As compared to subjects without necrosis, subjects with necrosis tended to be female, have chronic kidney disease, and shorter symptom onset to admission. The incidence of severe coronary artery disease was not significantly different between those with and without necrosis. 3/14 (21 .4%) subjects with myocyte necrosis showed evidence of acute myocardial infarction defined as ≥ 1 cm2 area of necrosis while 11/14 (78.6%) showed evidence of focal myocyte necrosis. Cardiac thrombi were present in 11/14 (78.6%) cases with necrosis, with 2/14 (14.2%) having epicardial coronary artery thrombi while 9/14 (64.3%) had microthrombi in myocardial capillaries, arterioles, and small muscular arteries. The most common pathologic cause of myocyte necrosis was microthrombi. Microthrombi were different in composition as compared to intramyocardial thromboemboli from COVID-19 negative subjects and to coronary thrombi retrieved from COVID-19 positive and negative STEMI patients. Tailored anti-thrombotic strategies may be useful to counteract the cardiac effects of COVID-19 infection.

Diagnostics & Screening

 Evaluation of Abbott BinaxNOW Rapid Antigen Test for SARS-CoV-2 Infection at Two Community-Based Testing Sites — Pima County, Arizona, November 3–17, 2020. Prince-Guerra JL, Almendares O, Nolen LD, et al. MMWR Morb Mortal Wkly Rep. ePub: 19 January 2021. DOI: <u>http://dx.doi.org/10.15585/mmwr.mm7003e3</u>

Findings: The BinaxNOW rapid antigen test received Emergency Use Authorization by the Food and Drug Administration for testing specimens from symptomatic persons; performance among asymptomatic persons is not well characterized. Sensitivity of the BinaxNOW antigen test, compared with polymerase chain reaction testing, was lower when used to test specimens from asymptomatic (35.8%) than from symptomatic (64.2%) persons, but specificity was high. Sensitivity was higher for culture-positive specimens (92.6% and 78.6% for those from symptomatic and asymptomatic persons, respectively); however, some antigen test-negative specimens had culturable virus. The high specificity and rapid BinaxNOW antigen test turnaround time facilitate earlier isolation of infectious persons. Antigen tests can be an important tool in an overall community testing strategy to reduce transmission.

9. Suitcase Lab for Rapid Detection of SARS-CoV-2 Based on Recombinase Polymerase Amplification Assay. El Wahed AA, Patel P, Maier M, et al. Anal Chem. 2021 Jan 20. doi: 10.1021/acs.analchem.0c04779. https://pubs.acs.org/doi/10.1021/acs.analchem.0c04779 Findings: Molecular real-time polymerase chain reaction (PCR) assays are very sensitive but require highly equipped laboratories and well-trained personnel. In this study, a rapid point-ofneed detection method was developed to detect the RNA-dependent RNA polymerase (RdRP), envelope protein (E), and nucleocapsid protein (N) genes of SARS-CoV-2 based on the reverse transcription recombinase polymerase amplification (RT-RPA) assay. RdRP, E, and N RT-RPA assays required approximately 15 min to amplify 2, 15, and 15 RNA molecules of molecular standard/reaction, respectively. RdRP and E RT-RPA assays detected SARS-CoV-1 and 2 genomic RNA, whereas the N RT-RPA assay identified only SARS-CoV-2 RNA. All established assays did not cross-react with nucleic acids of other respiratory pathogens. The RT-RPA assay's clinical sensitivity and specificity in comparison to real-time RT-PCR (n = 36) were 94 and 100% for RdRP; 65 and 77% for E; and 83 and 94% for the N RT-RPA assay. The assays were deployed to the field, where the RdRP RT-RPA assays confirmed to produce the most accurate results in three different laboratories in Africa (n = 89). The RPA assays were run in a mobile suitcase laboratory to facilitate the deployment at point of need. The assays can contribute to speed up the control measures as well as assist in the detection of COVID-19 cases in low-resource settings.

10. Factors Associated with US Public Motivation to Use and Distribute COVID-19 Self-tests. Bien-

Gund C, Dugosh K, Acri T, et al. *JAMA Netw Open*. 2021 Jan 4;4(1):e2034001. doi: 10.1001/jamanetworkopen.2020.34001.

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775297

Findings: We found that the majority of survey participants were motivated to distribute COVID-19 self-test kits and to use self-test kits. Motivation is a prerequisite for voluntary behavior, and our findings suggest that the secondary distribution of COVID-19 self-test kits may be associated with increased test uptake and case detection. However, individuals with lower socioeconomic status reported lower motivation and may be less likely to distribute test kits and self-test; behavioral interventions may help increase motivation in this population. Limitations include use of online sampling methods, which may limit generalizability of prevalence estimates and introduce sampling bias; however, observed associations from MTurk sampling are often comparable to those obtained by conventional survey methods. In addition, we did not assess behavioral outcomes, and social desirability may be present with self-report data. Nonetheless, measures of motivation have been shown to more accurately predict health behavior than alternative variables.

Epidemiology & Public Health

Introduction of the South African SARS-CoV-2 variant 501Y.V2 into the UK. Tang JW, Toovey OTR, Harvey KN, Hui DDS. J Infect. 2021 Jan 17:S0163-4453(21)00030-X. doi: 10.1016/j.jinf.2021.01.007. <u>https://www.journalofinfection.com/article/S0163-4453(21)00030-X/fulltext</u>

The current surge of COVID-19 cases across the UK is now thought to be mostly driven by a new, highly transmissible SARS-CoV-2 variant (B.1.1.7/ VUI-202012/01),1 but another highly transmissible SARS-CoV-2 variant (B.1.351/501Y.V2) from South Africa has already been detected in the UK population [https://cov-lineages.org/global report.html]. This South African 501Y.V2 variant is characterised by three mutations in the SARS-CoV-2 spike (S) protein: K417N (a lysine to asparagine substitution at amino acid position 417 in the S protein), E484K (a glutamic acid to lysine substitution at amino acid position 501 in the S protein) and N501Y (an asparagine to tyrosine substitution at amino acid position 501 in the S protein). This last mutation is also present in the UK VUI-202012/01 variant.1

12. Emergence of SARS-CoV-2 B.1.1.7 Lineage - United States, December 29, 2020-January 12,

2021. Galloway SE, Paul P, MacCannell DR, et al. *MMWR Morb Mortal Wkly Rep.* 2021 Jan 22;70(3):95-99. doi: 10.15585/mmwr.mm7003e2.

https://www.cdc.gov/mmwr/volumes/70/wr/mm7003e2.htm

Findings: On December 14, 2020, the United Kingdom reported a SARS-CoV-2 variant of concern (VOC), lineage B.1.1.7, also referred to as VOC 202012/01 or 20I/501Y.V1. The B.1.1.7 variant is estimated to have emerged in September 2020 and has quickly become the dominant circulating SARS-CoV-2 variant in England (1). B.1.1.7 has been detected in over 30 countries, including the United States. As of January 13, 2021, approximately 76 cases of B.1.1.7 have been detected in 12 U.S. states. Multiple lines of evidence indicate that B.1.1.7 is more efficiently transmitted than are other SARS-CoV-2 variants. The modeled trajectory of this

variant in the U.S. exhibits rapid growth in early 2021, becoming the predominant variant in March. Increased SARS-CoV-2 transmission might threaten strained health care resources, require extended and more rigorous implementation of public health strategies, and increase the percentage of population immunity required for pandemic control. Taking measures to reduce transmission now can lessen the potential impact of B.1.1.7 and allow critical time to increase vaccination coverage. Collectively, enhanced genomic surveillance combined with continued compliance with effective public health measures, including vaccination, physical distancing, use of masks, hand hygiene, and isolation and quarantine, will be essential to limiting the spread of SARS-CoV-2, the virus that causes COVID-19. Strategic testing of persons without symptoms but at higher risk of infection, such as those exposed to SARS-CoV-2 or who have frequent unavoidable contact with the public, provides another opportunity to limit ongoing spread.

13. COVID-19 Trends Among Persons Aged 0-24 Years - United States, March 1-December 12, 2020. Leidman E, Duca LM, Omura JD, et al. *MMWR Morb Mortal Wkly Rep.* 2021 Jan 22;70(3):88-94. doi: 10.15585/mmwr.mm7003e1.

https://www.cdc.gov/mmwr/volumes/70/wr/mm7003e1.htm

Findings: This analysis provides a critical update and expansion of previously published data, to include trends after fall school reopenings, and adds preschool-aged children (0-4 years) and college-aged young adults (18-24 years) (1). Among children, adolescents, and young adults, weekly incidence (cases per 100,000 persons) increased with age and was highest during the final week of the review period (the week of December 6) among all age groups. Time trends in weekly reported incidence for children and adolescents aged 0-17 years tracked consistently with trends observed among adults since June, with both incidence and positive test results tending to increase since September after summer declines. Reported incidence and positive test results among children aged 0-10 years were consistently lower than those in older age groups. To reduce community transmission, which will support schools in operating more safely for in-person learning, communities and schools should fully implement and strictly adhere to recommended mitigation strategies, especially universal and proper masking, to reduce COVID-19 incidence.

14. The Proportion of SARS-CoV-2 Infections That Are Asymptomatic: A Systematic Review. Oran DP, Topol EJ. Ann Intern Med. 2021 Jan 22. doi: 10.7326/M20-6976.

https://www.acpjournals.org/doi/10.7326/M20-6976

Findings: Sixty-one eligible studies and reports were identified, of which 43 used PCR testing of nasopharyngeal swabs to detect current SARS-CoV-2 infection and 18 used antibody testing to detect current or prior infection. In the 14 studies with longitudinal data that reported information on the evolution of symptomatic status, nearly three quarters of persons who tested positive but had no symptoms at the time of testing remained asymptomatic. The highest-quality evidence comes from nationwide, representative serosurveys of England (n = 365 104) and Spain (n = 61 075), which suggest that at least one third of SARS-CoV-2 infections are asymptomatic. Available data suggest that nearly three quarters of persons who receive a positive PCR test result but have no symptoms at the time of testing will remain asymptomatic.

Control strategies for COVID-19 should be altered, taking into account the prevalence and transmission risk of asymptomatic SARS-CoV-2 infection.

Healthcare Delivery & Healthcare Workers

15. Mobile Integrated Health Care in Los Angeles: Upstream Solutions to Mitigate the Covid-19 Pandemic. *NEJM Catalyst* 2021 Feb. doi: https://doi.org/10.1056/CAT.20.0383 https://catalyst.nejm.org/doi/full/10.1056/CAT.20.0383

In many communities, the local 911 emergency medical service (EMS) operator may be the largest provider of acute, unscheduled health care. In the City of Los Angeles, for example, the Los Angeles Fire Department (LAFD) is the sole provider of 911 care and in 2019 received more than 1.1 million calls for help and attended more than 400,000 incidents, treating/releasing more than 135,000 patients on scene and transporting 600-plus patients to area hospitals each day. As the upstream triage and treatment provider for 70 different area hospitals serving a population of 4 million, LAFD has a unique geographic view of public health problems and practices medicine directly in the patient's home (be it a mansion, single-room occupancy, jail cell, or tent). With most patient encounters, emergency medical technicians (EMTs) and paramedics practice shared decision-making with patients as they decide, "Do I go to the hospital, go somewhere else on my own, or do nothing?"

16. Reports of Forgone Medical Care Among US Adults During the Initial Phase of the COVID-19 Pandemic. Anderson KE, McGinty EE, Presskreischer R, Barry CL. *JAMA Netw Open*. 2021 Jan 4;4(1):e2034882. doi: 10.1001/jamanetworkopen.2020.34882.

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775366

Findings: This survey study used data from the second wave of the Johns Hopkins COVID-19 Civic Life and Public Health Survey, fielded from July 7 to July 22, 2020. The primary outcomes were missed doses of prescription medications; forgone preventive and other general medical care, mental health care, and elective surgeries; forgone care for new severe health issues; and reasons for forgoing care. The sample of respondents included 691 (52%) women, 840 non-Hispanic White individuals (63%), 160 non-Hispanic Black individuals (12%), and 223 Hispanic individuals (17%). The mean (SE) age of respondents was 48 (0.78) years. A total of 544 respondents (41%) forwent medical care from March through mid-July 2020. Among 1055 individuals (79%) who reported needing care, 544 (52%) reported forgoing care for any reason, 307 (29%) forwent care owing to fear of SARS-CoV-2 transmission, and 75 (7%) forwent care owing to financial concerns associated with the COVID-19 pandemic. Respondents who were unemployed, compared with those who were employed, forwent care more often (121 of 186 respondents [65%] vs 251 of 503 respondents [50%]; P = .01) and were more likely to attribute forgone care to fear of SARS-CoV-2 transmission (78 of 186 respondents [42%] vs 120 of 503 respondents [24%]; P = .002) and financial concerns (36 of 186 respondents [20%] vs 28 of 503 respondents [6%]; P = .001). Respondents lacking health insurance were more likely to attribute forgone care to financial concerns than respondents with Medicare or commercial coverage (19 of 88 respondents [22%] vs 32 of 768 respondents [4%]; P < .001). Frequency of and reasons for forgone care differed in some instances by race/ethnicity, socioeconomic status, age, and health status. This survey study found a high frequency of forgone care among US adults from

March to mid-July 2020. Policies to improve health care affordability and to reassure individuals that they can safely seek care may be necessary with surging COVID-19 case rates.

- 17. COVID-19 and healthcare workers: a rapid systematic review into risks and preventive measures. Gross JV, Mohren J, Erren TC. BMJ Open. 2021 Jan 20;11(1):e042270. doi: 10.1136/bmjopen-2020-042270. https://bmjopen.bmj.com/content/11/1/e042270 Findings: 27 studies were identified as relevant for exploring the risk of infection, 11 studies evaluated preventive measures. The studies described that SARS-CoV-2 impacts significantly on HCW's health and well-being, not only through infections (n=6), but also from a mental health perspective (n=16). 4 studies reported indirect risks such as skin injuries, one study described headaches to result from the use of personal protective equipment. Few studies provided information on the effectiveness of prevention strategies. Overall, most studies on health risks as well as on the effectiveness of preventive measures were of a moderate-to-low quality; this was mainly due to limitations in study design, imprecise exposure and outcome assessments. Due to widespread exposure of HCW to SARS-CoV-2, workplaces in healthcare must be as safe as possible. Information from HCW can provide valuable insights into how infections spread, into direct and indirect health effects and into how effectively counter-measures mitigate adverse health outcomes. However, available research disallows to judge which countermeasure(s) of a current 'mix' should be prioritised for HCW. To arrive at evidence-based costeffective prevention strategies, more well-conceived studies on the effectiveness of countermeasures are needed.
- 18. Antibody persistence in the first six months following SARS-CoV-2 infection among hospital workers: a prospective longitudinal study. L'Huillier AG, Meyer B, Andrey DO, et al. *Clin Microbiol Infect.* 2021 Jan 19:S1198-743X(21)00031-8. doi: 10.1016/j.cmi.2021.01.005. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7816882/ Findings: SARS-CoV-2-specific antibodies persisted in all participants up to 6 months. Neutralizing antibodies were detectable in 99.5% (195/196) of participants at six months post infection. Neutralizing antibodies persisted at six months in almost all participants, indicating more durability than initially feared. Anti-RBD antibodies persisted better and even increased over time, possibly related to the preferential detection of progressively higher-affinity antibodies.

Prognosis

19. COVID-19 Infection among US Dialysis Patients: Risk Factors and Outcomes from a National Dialysis Provider. Hsu CM, Weiner DE, Aweh G, et al *Am J Kidney Dis.* 2021 Jan 16:S0272-6386(21)00025-1. doi: 10.1053/j.ajkd.2021.01.003. <u>https://www.ajkd.org/article/S0272-6386(21)00025-1/fulltext</u>

Findings: 438/7948 (5.5%) maintenance dialysis patients developed COVID-19. Male sex, Black race, in-center dialysis (vs. home dialysis), treatment at an urban clinic, residence in a congregate setting, and greater comorbidity were associated with contracting COVID-19. Odds of COVID-19 was 17-fold higher for those residing in a congregate setting. Of the 438 maintenance dialysis patients with COVID-19, 109 (24.9%) died. Older age, heart disease, and

markers of frailty were associated with mortality. COVID-19 is common among patients receiving maintenance dialysis, particularly those residing in congregate settings. Among maintenance dialysis patients with COVID-19, mortality is high, exceeding 20%.

20. Association of Smoking and Cumulative Pack-Year Exposure with COVID-19 Outcomes in the Cleveland Clinic COVID-19 Registry. Lowe KE, Zein J, Hatipoğlu U, et al. JAMA Intern Med. January 25, 2021. doi:10.1001/jamainternmed.2020.8360

https://jamanetwork.com/journals/jamainternalmedicine/newonline

Findings: The results of this study suggest that cumulative exposure to cigarette smoke is an independent risk factor for hospital admission and death from COVID-19. Smoking is imperfectly classified in patient electronic medical records, and former smokers are potentially classified as never smokers, while pack-years may be underrecorded. However, this misclassification is likely to bias the present results toward the null, which would underestimate the association of cigarette smoking on adverse COVID-19 outcomes. The limitations on who has access to care at tertiary medical centers in the United States prevent generalizability to the whole population. The patients with complete data in this study are likely to be wealthier and have more consistent access to health care, as pack-years of smoking was typically collected during previous visits to the Cleveland Clinic. Nevertheless, we have demonstrated in this single central registry of patients who tested positive for COVID-19 that increased cumulative smoking was associated with a higher risk of hospitalization and mortality from COVID-19 in a dosedependent manner.

21. Evaluation and improvement of the National Early Warning Score (NEWS2) for COVID-19: a multi-hospital study. Carr E, Bendayan R, Bean D, et al. *BMC Med.* 2021 Jan 21;19(1):23. doi: 10.1186/s12916-020-01893-3.

https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-020-01893-3

Findings: A baseline model of 'NEWS2 + age' had poor-to-moderate discrimination for severe COVID-19 infection at 14 days. A supplemented model adding eight routinely collected blood and physiological parameters (supplemental oxygen flow rate, urea, age, oxygen saturation, C-reactive protein, estimated glomerular filtration rate, neutrophil count, neutrophil/lymphocyte ratio) improved discrimination, and these improvements were replicated across seven UK and non-UK sites. However, there was evidence of miscalibration with the model tending to underestimate risks in most sites. NEWS2 score had poor-to-moderate discrimination for medium-term COVID-19 outcome which raises questions about its use as a screening tool at hospital admission. Risk stratification was improved by including readily available blood and physiological parameters measured at hospital admission, but there was evidence of miscalibration in external sites. This highlights the need for a better understanding of the use of early warning scores for COVID.

22. Vitamin D supplementation, COVID-19 & Disease Severity: A meta-analysis. Shah K, Saxena D, Mavalankar D. QJM. 2021 Jan 24:hcab009. doi: 10.1093/qjmed/hcab009. https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcab009/6118232 Findings: Initially, it was observed that the COVID-19 patients with vitamin D deficiency had poorer outcomes with longer stay in the ICU and are at higher mortality rates than their counterparts8. Numerous attempts in the form of systematic reviews and meta-analysis to assess the potential role of vitamin D deficiency in COVID-19 infection, severity and mortality. However majority of the reviews remained inconclusive and highlighted the need for more primary studies in the form of randomized controlled trials. Similarly, unlike other respiratory tract diseases, evidence showing effect of supplementation of Oral VitD on improving the outcome of COVID-19 is still limited to few trials with smaller sample size. Current meta-analysis aimed to synthesize cumulative evidences from the studies reporting the effect of vitamin D supplementation on ICU stay and mortality outcomes in patients suffering from COVID-19 infections.

23. Use of non-steroidal anti-inflammatory drugs and risk of death from COVID-19: an OpenSAFELY cohort analysis based on two cohorts. Wong AY, MacKenna B, Morton CE, et al. Ann Rheum Dis. 2021 Jan 21:annrheumdis-2020-219517. doi: 10.1136/annrheumdis-2020-219517. https://ard.bmj.com/content/early/2021/01/20/annrheumdis-2020-219517 Findings: We conducted two cohort studies from 1 March to 14 June 2020 using routine clinical data in England linked to death data. In study 1, we identified people with an NSAID prescription in the last 3 years from the general population. In study 2, we identified people with rheumatoid arthritis/osteoarthritis. We defined exposure as current NSAID prescription within the 4 months before 1 March 2020. We used Cox regression to estimate HRs for COVID-19 related death in people currently prescribed NSAIDs, compared with those not currently prescribed NSAIDs, accounting for age, sex, comorbidities, other medications and geographical region. In study 1, we included 536 423 current NSAID users and 1 927 284 non-users in the general population. We observed no evidence of difference in risk of COVID-19 related death associated with current use in the multivariable-adjusted model. In study 2, we included 1 708 781 people with rheumatoid arthritis/osteoarthritis, of whom 175 495 (10%) were current NSAID users. In the multivariable-adjusted model, we observed a lower risk of COVID-19 related death associated with current use of NSAID versus non-use. We found no evidence of a harmful effect of routinely prescribed NSAIDs on COVID-19 related deaths. Risks of COVID-19 do not need to influence decisions about the routine therapeutic use of NSAIDs.

24. OUTCOMES AFTER VASCULAR SURGERY PROCEDURES IN PATIENTS WITH COVID-19 INFECTION: A NATIONAL MULTICENTRE COHORT STUDY (COVID-VAS). Spanish Society of Angiology and Vascular Surgery (SEACV). Ann Vasc Surg. 2021 Jan 22:S0890-5096(21)00054-6. doi: 10.1016/j.avsg.2021.01.054. <u>https://www.annalsofvascularsurgery.com/article/S0890-5096(21)00054-6/pdf</u>

Findings: We analyzed data from 75 patients with COVID-19 infection undergoing vascular surgery procedures in 17 hospitals across Spain and Andorra between March and May 2020. The mean age was 70.9 (45-94) and 58 (77.0%) patients were male. 70.7% had postoperative complications, 36.0% of patients experienced respiratory failure, 22.7% acute renal failure and 22.7% acute respiratory distress syndrome (ARDS). All-cause 30-days mortality rate was 37.3%. Patients with COVID-19 infection undergoing vascular surgery procedures showed poor 30-days survival. Age>65 years, preoperative lymphocytes <0.6 (x109/L) and LDH>500 (UI/L), and postoperative acute renal failure, ARDS and need for major amputation were identified as prognostic factors of 30-days mortality.

25. Asthma in Adult Patients with COVID-19: Prevalence and Risk of Severe Disease. Terry PD, Heidel RE, Dhand R. Am J Respir Crit Care Med. 2021 Jan 25. doi: 10.1164/rccm.202008-3266OC. https://www.atsjournals.org/doi/abs/10.1164/rccm.202008-3266OC Findings: We identified 147 studies worldwide that allowed us to compare the prevalence of asthma in patients with COVID-19 by region, disease severity and mortality. The results of our analyses do not provide clear evidence of increased risk of COVID-19 diagnosis, hospitalization or severity, due to asthma. These findings could provide some reassurance to people with asthma regarding its potential to increase their risk of severe morbidity from COVID-19.

Therapeutics

26. Impact of high dose prophylactic anticoagulation in critically ill patients with COVID-19 pneumonia. Tacquard C, Mansour A, Godon A, et al. *Chest.* 2021 Jan 16:S0012-3692(21)00047-7. doi: 10.1016/j.chest.2021.01.017. <u>https://journal.chestnet.org/article/S0012-3692(21)00047-7/fulltext</u>

Findings: All consecutive patients referred to eight French intensive care units (ICU) for COVID-19 were included in our observational study. Out of 538 patients included, 104 patients developed a total of 122 TC with an incidence of 22.7 % (19.2-26.3). Pulmonary embolism accounted for 52 % of the recorded TC. High dose prophylactic anticoagulation was associated with a significant reduced risk of TC without increasing the risk of bleeding. High dose prophylactic anticoagulation is associated with a reduction in thrombotic complications in critically ill COVID-19 patients without an increased risk of hemorrhage. Randomized controlled trials comparing prophylaxis with higher doses of anticoagulants are needed to confirm these results.

27. Effect of Discontinuing vs Continuing Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers on Days Alive and Out of the Hospital in Patients Admitted With COVID-19: A Randomized Clinical Trial. BRACE CORONA Investigators. *JAMA*. 2021 Jan 19;325(3):254-264. doi: 10.1001/jama.2020.25864.

https://jamanetwork.com/journals/jama/fullarticle/2775280

Findings: Among 659 patients, the median age was 55.1 years, 14.7% were aged 70 years or older, 40.4% were women, and 100% completed the trial. The median time from symptom onset to hospital admission was 6 days and 27.2% of patients had an oxygen saturation of less than 94% of room air at baseline. Among patients hospitalized with mild to moderate COVID-19 and who were taking ACEIs or ARBs before hospital admission, there was no significant difference in the mean number of days alive and out of the hospital for those assigned to discontinue vs continue these medications. These findings do not support routinely discontinuing ACEIs or ARBs among patients hospitalized with mild to moderate COVID-19 if there is an indication for treatment.

28. Lower or Higher Oxygenation Targets for Acute Hypoxemic Respiratory Failure. HOT-ICU Investigators. *N Engl J Med*. 2021 Jan 20. doi: 10.1056/NEJMoa2032510. <u>https://www.nejm.org/doi/full/10.1056/NEJMoa2032510</u> Findings: In this multicenter trial, we randomly assigned 2928 adult patients who had recently been admitted to the ICU and who were receiving at least 10 liters of oxygen per minute in an open system or had a fraction of inspired oxygen of at least 0.50 in a closed system to receive oxygen therapy targeting a Pao2 of either 60 mm Hg (lower-oxygenation group) or 90 mm Hg (higher-oxygenation group) for a maximum of 90 days. The primary outcome was death within 90 days. At 90 days, 618 of 1441 patients (42.9%) in the lower-oxygenation group and 613 of 1447 patients (42.4%) in the higher-oxygenation group had died. At 90 days, there was no significant between-group difference in the percentage of days that patients were alive without life support or in the percentage of days they were alive after hospital discharge. The percentages of patients who had new episodes of shock, myocardial ischemia, ischemic stroke, or intestinal ischemia were similar in the two groups (P = 0.24). Among adult patients with acute hypoxemic respiratory failure in the ICU, a lower oxygenation target did not result in lower mortality than a higher target at 90 days.

29. Extracorporeal Membrane Oxygenation for COVID-19 respiratory distress syndrome: an Italian Society for Cardiac Surgery Report. Loforte A, Di Mauro M, Pellegrini C, et al. ASAIO J. 2021 Jan 18. doi: 10.1097/MAT.00000000001399.

https://journals.lww.com/asaiojournal/Abstract/9000/Extracorporeal Membrane Oxygenation for COVID 19.98380.aspx

Findings: Between March 1st and September 15th, 2020, a veno-venous (VV) ECMO system was installed in 67 patients (94%) and a veno-arterio-venous (VAV) ECMO in four (6%). Five patients required VA ECMO after initial weaning from VV ECMO. Thirty (42.2%) patients were weaned from ECMO, while 39 (54.9%) died on ECMO, and six (8.5%) died after ECMO removal. Overall hospital survival was 36.6% (n=26). Main causes of death were multiple organ failure (n=14, 31.1%) and sepsis (n=11, 24.4%). On multivariable analysis, predictors of death while on ECMO support were older age (p=0.048), elevated pre-ECMO C-reactive protein level (p=0.048), higher positive end-expiratory pressure on ventilator (p=0.036) and lower lung compliance (p=0.032). If the conservative treatment is not effective, ECMO support might be considered as life-saving rescue therapy for COVID-19 refractory respiratory failure. However warm caution and thoughtful approaches for timely detection and treatment should be taken for such a delicate patient population.

30. Effect of tocilizumab on clinical outcomes at 15 days in patients with severe or critical coronavirus disease 2019: randomised controlled trial. Veiga VC, Prats JAGG, Farias DLC, et al.

BMJ 2021; 372 :n84 <u>https://www.bmj.com/content/372/bmj.n84</u> Findings: A total of 129 patients were enrolled (mean age 57 years; 68% men) and all completed follow-up. All patients in the tocilizumab group and two in the standard care group received tocilizumab. 18 of 65 (28%) patients in the tocilizumab group and 13 of 64 (20%) in the standard care group were receiving mechanical ventilation or died at day 15 (odds ratio 1.54, 95% confidence interval 0.66 to 3.66; P=0.32). Death at 15 days occurred in 11 (17%) patients in the tocilizumab group compared with 2 (3%) in the standard care group (odds ratio 6.42, 95% confidence interval 1.59 to 43.2). Adverse events were reported in 29 of 67 (43%) patients who received tocilizumab and 21 of 62 (34%) who did not receive tocilizumab. In patients with severe or critical covid-19, tocilizumab plus standard care was not superior to standard care alone in improving clinical outcomes at 15 days, and it might increase mortality.

- 31. Intermediate-dose anticoagulation, aspirin, and in-hospital mortality in COVID-19: a propensity score-matched analysis. Meizlish ML, Goshua G, Liu Y, et al. Am J Hematol. 2021 Jan 21. doi: 10.1002/ajh.26102. https://onlinelibrary.wiley.com/doi/10.1002/ajh.26102
 Findings: We examined in-hospital mortality with intermediate- compared to prophylactic-dose anticoagulation, and separately with in-hospital aspirin compared to no antiplatelet therapy, in a large, retrospective study of 2785 hospitalized adult COVID-19 patients. Among propensity-score matched patients in the aspirin cohort (N = 638), in a multivariable regression model, in-hospital aspirin compared to no antiplatelet therapy was associated with a significantly lower cumulative incidence of in-hospital death. In this propensity score-matched, observational study of COVID-19, intermediate-dose anticoagulation and aspirin were each associated with a lower cumulative incidence of in-hospital death.
- 32. **Treatment of Severe COVID-19 with Convalescent Plasma in Bronx, NYC.** Yoon HA, Bartash R, Gendlina I, et al. *JCI Insight*. 2021 Jan 21:142270. doi: 10.1172/jci.insight.142270. https://insight.jci.org/articles/view/142270

Findings: We compared the mortality and clinical outcome of patients with COVID-19 who received 200mL of CCP with a Spike protein IgG titer ≥1:2,430 within 72 hours of admission to propensity score-matched controls cared for at a medical center in the Bronx, between April 13 to May 4, 2020. There was no difference in mortality or oxygenation between CCP recipients and controls at day 28. When stratified by age, compared to matched controls, CCP recipients <65 years had 4-fold lower mortality and 4-fold lower deterioration in oxygenation or mortality at day 28. For CCP recipients, pre-transfusion Spike protein IgG, IgM and IgA titers were associated with mortality at day 28 in univariate analyses. No adverse effects of CCP were observed. Our results suggest CCP may be beneficial for hospitalized patients <65 years, but data from controlled trials is needed to validate this finding and establish the effect of ageing on CCP efficacy.

33. Effect of Bamlanivimab as Monotherapy or in Combination with Etesevimab on Viral Load in Patients with Mild to Moderate COVID-19: A Randomized Clinical Trial. Gottlieb RL, Nirula A, Chen P, et al. *JAMA*. 2021 Jan 21. doi: 10.1001/jama.2021.0202.

https://jamanetwork.com/journals/jama/fullarticle/2775647

Findings: The BLAZE-1 study is a randomized phase 2/3 trial at 49 US centers including ambulatory patients (N = 613) who tested positive for SARS-CoV-2 infection and had 1 or more mild to moderate symptoms. Patients were randomized to receive a single infusion of bamlanivimab (700 mg [n = 101], 2800 mg [n = 107], or 7000 mg [n = 101]), the combination treatment (2800 mg of bamlanivimab and 2800 mg of etesevimab [n = 112]), or placebo (n = 156) Among the 577 patients who were randomized and received an infusion (mean age, 44.7, 54.6% women), 533 (92.4%) completed the efficacy evaluation period (day 29). Among nonhospitalized patients with mild to moderate COVID-19 illness, treatment with bamlanivimab and etesevimab, compared with placebo, was associated with a statistically significant reduction in SARS-CoV-2 viral load at day 11; no significant difference in viral load reduction was observed for bamlanivimab monotherapy. Further ongoing clinical trials will focus on assessing the clinical benefit of antispike neutralizing antibodies in patients with COVID-19 as a primary end point.

34. Early Use of Corticosteroid May Prolong SARS-CoV-2 Shedding in Non-Intensive Care Unit Patients with COVID-19 Pneumonia: A Multicenter, Single-Blind, Randomized Control Trial. Tang X, Feng YM, Ni JX, et al. *Respiration*. 2021 Jan 22:1-11. doi: 10.1159/000512063. https://www.karger.com/Article/FullText/512063

Findings: This was a prospective, multicenter, single-blind, randomized control trial. Adult patients with COVID-19 pneumonia who were admitted to the general ward were randomly assigned to either receive methylprednisolone or not for 7 days. A total of 86 COVID-19 patients underwent randomization. There was no difference of the incidence of clinical deterioration between the methylprednisolone group and control group (4.8 vs. 4.8%, p = 1.000). The duration of throat viral RNA detectability in the methylprednisolone group was 11 days, which was significantly longer than that in the control group (8 days [2-12 days], p = 0.030). There were no significant differences between the 2 groups in other secondary outcomes. Mass cytometry discovered CD3+ T cells, CD8+ T cells, and NK cells in the methylprednisolone group which were significantly lower than those in the control group after randomization (p < 0.05). From this prematurely closed trial, we found that the short-term early use of corticosteroid could suppress the immune cells, which may prolong severe acute respiratory syndrome coronavirus 2 shedding in patients with COVID-19 pneumonia.

35. Mortality Risk Assessment in Covid-19 Veno-Venous Extracorporeal Membrane Oxygenation. Tabatabai A, Ghneim MH, Kaczorowski DJ, et al. *Ann Thorac Surg.* 2021 Jan 21:S0003-4975(21)00104-1. doi: 10.1016/j.athoracsur.2020.12.050.

https://www.clinicalkey.com/#!/content/journal/1-s2.0-S0003497521001041

Findings: Forty COVID-19 ECMO patients were identified. Of the 33 patients (82.5%) off ECMO at time of analysis, 18 patients (54.5%) survived to hospital discharge and 15 (45.5%) died on ECMO. Non-survivors presented with a statistically significant higher Prediction of Survival on ECMO Therapy (PRESET)-Score (mean \pm standard deviation 8.33 \pm 0.8 vs. 6.17 \pm 1.8, P = 0.001). The PRESET-Score demonstrated accurate mortality prediction. All patients with a PRESET-Score of \leq 6 survived, and a score \geq 7 was associated with a dramatic increase in mortality. These results suggest favorable outcomes are possible in COVID-19 ECMO patients at high volume centers. This study is the first to demonstrate an association between the PRESET-Score and survival in COVID-19 VV-ECMO patients. Standard risk calculators may aid in appropriate COVID-19 ARDS patient selection for ECMO.

36. Rate control in atrial fibrillation using Landiolol is safe in critically ill Covid-19 patients. Hariri

G, Urbina T, Mazerand S, et al. *Crit Care.* 2021 Jan 22;25(1):33. doi: 10.1186/s13054-021-03470-3. <u>https://ccforum.biomedcentral.com/articles/10.1186/s13054-021-03470-3</u> Findings: Landiolol is a beta-blocker with highly β 1 selective activity, used either in AF patients either to control heart rate or to prevent supraventricular arrhythmia occurrence in the context of cardiac surgery. Landiolol has an ultrashort half-life of 4 min and weaker negative inotropic effect compared with other intravenous β -blockers. A recent randomized controlled trial in patient with sepsis/septic shock developing tachyarrhythmia showed that Landiolol infusion efficiently reduced heart rate without any significant hemodynamic side effect. Here, we described in critically ill patients admitted to the ICU for SARS-CoV-2 infections presenting with AF, our experience of Landiolol use in terms of efficacy and safety.

37. Effect of anakinra versus usual care in adults in hospital with COVID-19 and mild-to-moderate pneumonia (CORIMUNO-ANA-1): a randomised controlled trial. CORIMUNO-19 Collaborative group. *Lancet Respir Med.* 2021 Jan 22:S2213-2600(20)30556-7. doi: 10.1016/S2213-2600(20)30556-7.

https://www.sciencedirect.com/science/article/pii/S2213260020305567?via%3Dihub Findings: Between April 8 and April 26, 2020, we screened 153 patients. The study was stopped early following the recommendation of the data and safety monitoring board, after the recruitment of 116 patients: 59 were assigned to the anakinra group, and 57 were assigned to the usual care group. Two patients in the usual care group withdrew consent and were not analysed. In the analysable population, the median age was 66 years (IQR 59 to 76) and 80 (70%) participants were men. In the anakinra group, 21 (36%) of 59 patients had a WHO-CPS score of more than 5 at day 4 versus 21 (38%) of 55 in the usual care group (median posterior absolute risk difference [ARD] -2.5%, 90% credible interval [Crl] -17.1 to 12.0), with a posterior probability of ARD of less than 0 (ie, anakinra better than usual care) of 61.2%. At day 14, 28 (47%; 95% CI 33 to 59) patients in the anakinra group and 28 (51%; 95% CI 36 to 62) in the usual care group needed ventilation or died, with a posterior probability of any efficacy of anakinra (hazard ratio [HR] being less than 1) of 54.5% (median posterior HR 0.97; 90% Crl 0.62 to 1.52). At day 90, 16 (27%) patients in the anakinra group and 15 (27%) in the usual care group had died. Serious adverse events occurred in 27 (46%) patients in the anakinra group and 21 (38%) in the usual care group (p=0.45). Anakinra did not improve outcomes in patients with mild-tomoderate COVID-19 pneumonia. Further studies are needed to assess the efficacy of anakinra in other selected groups of patients with more severe COVID-19.

 Thrombosis, Bleeding, and the Observational Effect of Early Therapeutic Anticoagulation on Survival in Critically III Patients with COVID-19. Al-Samkari H, Gupta S, Leaf RK, et al. Ann Intern Med. 2021 Jan 26. doi: 10.7326/M20-6739. <u>https://www.acpjournals.org/doi/10.7326/M20-6739</u>

Findings: In a multicenter cohort study of 3239 critically ill adults with COVID-19, the incidence of VTE and major bleeding within 14 days after ICU admission was evaluated. Among the 3239 patients included, the median age was 61 years (interquartile range, 53 to 71 years), and 2088 (64.5%) were men. A total of 204 patients (6.3%) developed VTE, and 90 patients (2.8%) developed a major bleeding event. Independent predictors of VTE were male sex and higher D-dimer level on ICU admission. Among the 2809 patients included in the target trial emulation, 384 (11.9%) received early therapeutic anticoagulation. In the primary analysis, during a median follow-up of 27 days, patients who received early therapeutic anticoagulation had a similar risk for death as those who did not. Among critically ill adults with COVID-19, early therapeutic anticoagulation did not affect survival in the target trial emulation.

 Higher anticoagulation targets and risk of thrombotic events in severe COVID-19 patients: bicenter cohort study. Helms J, Severac F, Merdji H, et al. Ann Intensive Care. 2021 Jan 25;11(1):14. doi: 10.1186/s13613-021-00809-5.

https://annalsofintensivecare.springeropen.com/articles/10.1186/s13613-021-00809-5 Findings: One hundred and seventy-nine patients (73% men) were analyzed: 108 in prophylactic group and 71 in therapeutic group. Fifty-seven patients developed clinically relevant thrombotic complications during their ICU stay, less frequently in therapeutic group. The occurrences of pulmonary embolism (PE), deep vein thrombosis (DVT) and ischemic stroke were significantly lower in the therapeutic group. The occurrence of bleeding complications was not significantly different between groups, neither were ICU length of stay or mortality rate. D-dimer levels were significantly lower during ICU stay, and aPTT ratio was more prolonged in the therapeutic group (p < 0.05). Increasing the anticoagulation of severe COVID-19 patients to a therapeutic level might decrease thrombotic complications without increasing their bleeding risk.

Transmission / Infection Control

- 40. Mask-wearing and control of SARS-CoV-2 transmission in the USA: a cross-sectional study. Rader B et al. Lancet 2021 Jan 19. https://doi.org/10.1016/S2589-7500(20)30293-4 Findings: Serial cross-sectional surveys were administered via a web platform to randomly surveyed US individuals aged 13 years and older, to query self-reports of face mask-wearing. 378 207 individuals responded to the survey between June 3 and July 27, 2020, of which 4186 were excluded for missing data. We observed an increasing trend in reported mask usage across the USA, although uptake varied by geography. A logistic model controlling for physical distancing, population demographics, and other variables found that a 10% increase in selfreported mask-wearing was associated with an increased odds of transmission control. We found that communities with high reported mask-wearing and physical distancing had the highest predicted probability of transmission control. Segmented regression analysis of reported mask-wearing showed no statistically significant change in the slope after mandates were introduced; however, the upward trend in reported mask-wearing was preserved. The widespread reported use of face masks combined with physical distancing increases the odds of SARS-CoV-2 transmission control. Self-reported mask-wearing increased separately from government mask mandates, suggesting that supplemental public health interventions are needed to maximise adoption and help to curb the ongoing epidemic.
- 41. Prophylaxis for COVID-19: a systematic review. Smit M, Marinosci A, Agoritsas T, et al. Clin Microbiol Infect. 2021 Jan 18:S1198-743X(21)00040-9. doi: 10.1016/j.cmi.2021.01.013. https://www.sciencedirect.com/science/article/pii/S1198743X21000409?dgcid=rss_sd_all Findings: We identified 13 studies and 117 RCTs meeting inclusion criteria. Non-RCT studies reported on cross-sectional studies using hydroxychloroquine (HCQ) in humans (n=2) or reported on animal studies (n=7) most of which used antibodies. All five completed RCTs focused on the use of HCQ as either PrEP or PEP and these and the cross-sectional studies reported no prophylactic effect. The majority of ongoing RCTs evaluated HCQ or other existing candidates including non-SARS-CoV-2 vaccines, anti(retro)virals, or use of vitamins and supplements. The key message from completed studies and RCTs seems to be that HCQ does

not work, there is little evidence regarding other compounds with all RCTs using candidates other than HCQ still ongoing. It remains to be seen if the portfolio of existing molecules being evaluated in RCTs will identify successful prophylaxis against COVID-19 or if there is a need for the development of new candidates.

- 42. Household transmission of SARS-CoV-2 and risk factors for susceptibility and infectivity in Wuhan: a retrospective observational study. Li F, Li YY, Liu MJ, et al. Lancet Infect Dis. 2021 Jan 18:S1473-3099(20)30981-6. doi: 10.1016/S1473-3099(20)30981-6. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30981-6/fulltext FINDINGS: 27 101 households with 29 578 primary cases and 57 581 household contacts were identified. The secondary attack rate estimated with the transmission model was 15.6%, assuming a mean incubation period of 5 days and a maximum infectious period of 22 days. Individuals aged 60 years or older were at a higher risk of infection with SARS-CoV-2 than all other age groups. Infants aged 0-1 years were significantly more likely to be infected than children aged 2-5 years and children aged 6-12 years. Given the same exposure time, children and adolescents younger than 20 years of age were more likely to infect others than were adults aged 60 years or older. Asymptomatic individuals were much less likely to infect others than were symptomatic cases. Symptomatic cases were more likely to infect others before symptom onset than after. Within households, children and adolescents were less susceptible to SARS-CoV-2 infection but were more infectious than older individuals. Presymptomatic cases were more infectious and individuals with asymptomatic infection less infectious than symptomatic cases. These findings have implications for devising interventions for blocking household transmission of SARS-CoV-2, such as timely vaccination of eligible children once resources become available.
- 43. Safe and Efficient Performance of Open Tracheostomies in Patients with COVID-19-the Fenestrated Technique. Okuyemi OT, Spinner A, Elkins T, et al. *JAMA Otolaryngol Head Neck Surg.* 2021 Jan 21. doi: 10.1001/jamaoto.2020.4432.

https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2775355

Findings: Tracheostomy plays an important role in ventilated patients by improving pulmonary toileting and ventilator weaning while reducing risks of airway stenosis from prolonged intubation. However, it is associated with a considerable aerosolization risk. Severe acute respiratory syndrome coronavirus 2, which is responsible for COVID-19, concentrates in the upper aerodigestive tract and is transmitted through droplets or aerosols from aerosol-generating procedures (AGPs) performed in this region. While these facts have driven recommendations for using negative-pressure rooms and higher-grade personal protective equipment, such as powered air-purifying respirators for AGPs, there has not been a published study specifically investigating a technique of open tracheostomy that could further reduce aerosolization risks and improve safety. We demonstrate a fenestrated technique of tracheostomy that minimizes aerosolization risks by reducing risk of accidental decannulation and stomal infections while creating a tight seal around the tracheostomy tube.

44. An Assessment of Outpatient Clinic Room Ventilation Systems and Possible Relationship to Disease Transmission. King KG, Delclos GL, Brown EL, et al. Am J Infect Control. 2021 Jan

21:S0196-6553(21)00023-7. doi: 10.1016/j.ajic.2021.01.011. https://www.clinicalkey.com/#!/content/journal/1-s2.0-S0196655321000237

Findings: Ventilation rates were measured in 105 outpatient clinic rooms categorized by services rendered. Building characteristics were evaluated as determinants of ventilation rates, and risk of disease transmission was estimated using the Gammaitoni-Nucci model. When compared to Standard 170, 10% of clinic rooms assessed did not meet the minimum requirement for general exam rooms, 39% did not meet the requirement for treatment rooms, 83% did not meet the requirement for procedure rooms or minor surgical procedures. Lower than standard air changes per hour were observed and could lead to an increased risk of spread of diseases when conducting advanced procedures and evaluating persons of interest for emerging infectious diseases. These findings are pertinent during the SARS-CoV-2 pandemic, as working guidelines are established for the healthcare community.

Vaccine

- 45. Optimizing vaccine allocation for COVID-19 vaccines: critical role of single-dose vaccination. Matrajt L, Eaton J, Leung T, et al. *medRxiv PREPRINT*. 2021 Jan 16:2020.12.31.20249099. doi: 10.1101/2020.12.31.20249099. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7814836/ Findings: Most COVID-19 vaccines require two doses, and current vaccine prioritization guidelines for COVID-19 vaccines assume full-dose vaccine deployment. However in the context of limited vaccine supply and an expanding pandemic, policymakers are considering single-dose vaccination as an alternative strategy. Using a mathematical model combined with optimization algorithms, we determined the optimal allocation with one and two doses of vaccine to minimize five metrics of disease burden under various degrees of viral transmission. Under low transmission, we show that the optimal allocation of vaccine critically depends on the level of single-dose efficacy (SDE). If the SDE is high, single-dose vaccination is optimal, preventing up to 36% more deaths than a strategy prioritizing full-dose vaccination for older adults first. With low or moderate SDE, mixed vaccination campaigns with coverage of all older adults with one dose are optimal. However, with modest or high transmission, vaccinating older adults first with two doses is best, preventing up to 41% more deaths than a single-dose vaccination given across all populations. Further, we show that maintaining social distancing interventions and speedy deployment are key for effective vaccination campaigns. Our work suggests that it is imperative to determine the efficacy and durability of single-dose vaccines, as mixed or singledose vaccination campaigns may have the potential to contain the pandemic much more quickly.
- 46. Neutralization of SARS-CoV-2 lineage B.1.1.7 pseudovirus by BNT162b2 vaccine-elicited human sera. Muik A, Wallisch A-K, Sänger B, et al. *bioRxiv PREPRINT*. 2021 Jan 19. doi: https://doi.org/10.1101/2021.01.18.426984

https://www.biorxiv.org/content/10.1101/2021.01.18.426984v1.full.pdf

Findings: Recently, a new SARS-CoV-2 lineage called B.1.1.7 has emerged in the United Kingdom that was reported to spread more efficiently than other strains. This variant has an unusually large number of mutations with 10 amino acid changes in the spike protein, raising concerns

that its recognition by neutralizing antibodies may be affected. Here, we 20 investigated SARS-CoV-2-S pseudoviruses bearing either the Wuhan reference strain or the B.1.1.7 lineage spike protein with sera of 16 participants in a previously reported trial with the mRNA-based COVID-19 vaccine BNT162b2. The immune sera had equivalent neutralizing titers to both variants. These data, together with the combined immunity involving humoral and cellular effectors induced by this vaccine, make it unlikely that the B.1.1.7 lineage will escape BNT162b2-mediated protection.

**see Moderna press release below re: B.1.1.7 variant

47. Impact of SARS-CoV-2 B.1.1.7 Spike variant on neutralisation potency of sera from individuals vaccinated with Pfizer vaccine BNT162b2. DA Collier, B Meng, IATM Ferreira, et al. medRxiv PREPRINT. 2021 Jan 20. doi: https://doi.org/10.1101/2021.01.19.21249840 Findings: Here we tested immune responses in patients 3 weeks following the first dose of the Pfizer BioNTech vaccine BNT162b2. We also tested neutralising antibody responses against pseudoviruses expressing wild type Spike proteins or expressing 3 key mutations present in B.1.1.7 (deletion 69/70, N501Y, A570D). IgG Spike antibody titres correlated well with neutralisation. We observed a range of neutralisation titres against wild type, with geometric mean titre (GMT) of 24. The vaccine sera exhibited a range of inhibitory dilutions giving 50% neutralisation (ID50) from <1:4 to 3449. However a lower proportion of participants over 80 years old achieved threshold neutralisation titre of >1:4 for 50% neutralisation as compared to those under 80 years old (8/15 versus 8/8 P=0.052) after the first dose. Neutralisation titres were not significantly impacted by the combination of three Spike mutations tested, but were reduced against the full set of Spike mutations present in the B.1.1.7 variant. The highest fold change was approxiamately 6 and the median fold change for the B.1.1.7 variant versus wild type was 3.85 (IQR 2.68-5.28). Further work is needed to establish the impact of these observations on real life vaccine efficacy.

**see Pfizer press release below re: B.1.1.7 variant

48. Allergic Reactions Including Anaphylaxis after Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine. Shimabukuro T, Nair N. *JAMA*. 2021 Jan 21. doi: 10.1001/jama.2021.0600. https://jamanetwork.com/journals/jama/fullarticle/2775646

Findings: During December 14 to 23, 2020, after administration of a reported 1 893 360 first doses of Pfizer-BioNTech COVID-19 vaccine (1 177 527 in women, 648 327 in men, and 67 506 with sex of recipient not reported),3 CDC identified 21 case reports submitted to VAERS that met Brighton Collaboration case definition criteria for anaphylaxis (Table), corresponding to an estimated rate of 11.1 cases per million doses administered. Four patients (19%) were hospitalized (including 3 in intensive care), and 17 (81%) were treated in an emergency department; 20 (95%) are known to have been discharged home or had recovered at the time of the report to VAERS. No deaths from anaphylaxis were reported.

49. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomised, phase 1 trial. Ella R, Vadrevu KM, Jogdand H, et al. *Lancet Infect Dis.* 2021 Jan 21:S1473-3099(20)30942-7. doi: 10.1016/S1473-3099(20)30942-7. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30942-7/fulltext

Findings: We did a double-blind, multicentre, randomised, controlled phase 1 trial to assess the safety and immunogenicity of BBV152 at 11 hospitals across India. Healthy adults aged 18-55 years who were deemed healthy by the investigator were eligible. Individuals with positive SARS-CoV-2 nucleic acid and/or serology tests were excluded. Participants were randomly assigned to receive either one of three vaccine formulations (3 μg with Algel-IMDG, 6 μg with Algel-IMDG, or 6 µg with Algel) or an Algel only control vaccine group. Block randomisation was done with a web response platform. Participants and investigators were masked to treatment group allocation. Two intramuscular doses of vaccines were administered on day 0 (the day of randomisation) and day 14. Primary outcomes were solicited local and systemic reactogenicity events at 2 h and 7 days after vaccination and throughout the full study duration, including serious adverse events. Among the enrolled participants, 100 each were randomly assigned to the three vaccine groups, and 75 were randomly assigned to the control group (Algel only). After both doses, solicited local and systemic adverse reactions were reported by 17 (17%; 95% Cl 10·5-26·1) participants in the 3 μ g with Algel-IMDG group, 21 (21%; 13·8-30·5) in the 6 μ g with Algel-IMDG group, 14 (14%; $8\cdot1-22\cdot7$) in the 6 μ g with Algel group, and ten (10%; $6\cdot9-23\cdot6$) in the Algel-only group. The most common solicited adverse events were injection site pain (17 [5%] of 375 participants), headache (13 [3%]), fatigue (11 [3%]), fever (nine [2%]), and nausea or vomiting (seven [2%]). All solicited adverse events were mild (43 [69%] of 62) or moderate (19 [31%]) and were more frequent after the first dose. One serious adverse event of viral pneumonitis was reported in the 6 μ g with Algel group, unrelated to the vaccine. Seroconversion rates (%) were 87.9, 91.9, and 82.8 in the 3 µg with Algel-IMDG, 6 µg with Algel-IMDG, and 6 µg with Algel groups, respectively. CD4+ and CD8+ T-cell responses were detected in a subset of 16 participants from both Algel-IMDG groups. BBV152 led to tolerable safety outcomes and enhanced immune responses. Both Algel-IMDG formulations were selected for phase 2 immunogenicity trials. Further efficacy trials are warranted. FUNDING: Bharat Biotech International.

50. mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants. Wu K, Werner AP, Moliva JI, et al. *bioRxiv PREPRINT* 2021.01.25.427948; doi: <u>https://doi.org/10.1101/2021.01.25.427948</u>

Findings: The Moderna mRNA-1273 vaccine has demonstrated ~94% efficacy in a Phase 3 study and has been approved under Emergency Use Authorization. The emergence of SARS-CoV-2 variants with mutations in the spike protein, most recently circulating isolates from the United Kingdom (B.1.1.7) and Republic of South Africa (B.1.351), has led to lower neutralization from convalescent serum by pseudovirus neutralization (PsVN) assays and resistance to certain monoclonal antibodies. Here, using two orthogonal VSV and lentivirus PsVN assays expressing spike variants of 20E (EU1), 20A.EU2, D614G-N439, mink cluster 5, B.1.1.7, and B.1.351 variants, we assessed the neutralizing capacity of sera from human subjects or non-human primates (NHPs) that received mRNA-1273. No significant impact on neutralization against the B.1.1.7 variant was detected in either case, however reduced neutralization was measured against the mutations present in B.1.351. Geometric mean titer (GMT) of human sera from clinical trial participants in VSV PsVN assay using D614G spike was 1/1852. VSV pseudoviruses with spike containing K417N-E484K-N501Y-D614G and full B.1.351 mutations resulted in 2.7 and 6.4-fold GMT reduction, respectively, when compared to the D614G VSV pseudovirus. Importantly, the VSV PsVN GMT of these human sera to the full B.1.351 spike variant was still 1/290, with all evaluated sera able to fully neutralize. Similarly, sera from NHPs immunized with 30 or 100µg of mRNA-1273 had VSV PsVN GMTs of ~ 1/323 or 1/404, respectively, against the full B.1.351 spike variant with a ~ 5 to 10-fold reduction compared to D614G. Individual mutations that are characteristic of the B.1.1.7 and B.1.351 variants had a similar impact on neutralization when tested in VSV or in lentivirus PsVN assays. Despite the observed decreases, the GMT of VSV PsVN titers in human vaccinee sera against the B.1.351 variant remained at ~1/300. Taken together these data demonstrate reduced but still significant neutralization against the full B.1.351 variant following mRNA-1273 vaccination.

Whole Person Care

51. Suicide Deaths During the COVID-19 Stay-at-Home Advisory in Massachusetts, March to May **2020.** Faust JS, Shah SB, Du C, Li SX, Lin Z, Krumholz HM. *JAMA Netw Open.* 2021 Jan 4;4(1):e2034273. doi: 10.1001/jamanetworkopen.2020.34273.

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775359

Findings: Many policy makers believe that shelter-in-place or stay-at-home policies could cause an increase in what are known as deaths of despair. During the pandemic period, the incident rate for suicide deaths in Massachusetts was 0.67 per 100 000 person-months vs 0.80 per 100 000 person-months during the corresponding period in 2019. Because data for 2019 and 2020 are preliminary, a sensitivity analysis including all deaths still pending final cause adjudication as of November 14, 2020, was performed. The number of suicide deaths during the stay-at-home period did not deviate from projected expectations using either preliminary data or an alternate scenario in which deaths pending investigation that exceeded the average remaining number of deaths that occurred during the corresponding period in 2015 to 2019 were ascribed to suicide. Decedent age and sex demographic characteristics were unchanged during the pandemic period compared with those during 2015 to 2019.

52. Suicide-Related Internet Searches during the Early Stages of the COVID-19 Pandemic in the US. Ayers JW, Poliak A, Johnson DC, et al. *JAMA Netw Open*. 2021 Jan 4;4(1):e2034261. doi:

10.1001/jamanetworkopen.2020.34261.

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775358

Findings: Experts anticipate that the societal fallout associated with the COVID-19 pandemic will increase suicidal behavior, and strategies to address this anticipated increase have been woven into policy decision-making without contemporaneous data. For instance, Donald Trump cited increased suicides as an argument against COVID-19 control measures during the first presidential debate on September 29, 2020. We found all queries containing the term *suicide* cumulatively decreased by 22% in the 18 weeks after President Trump declared a national emergency and never eclipsed their expected search rate for any week. In raw terms, this was approximately 7.8 million fewer searches than expected. Moreover, searches for 15 of the 20 related terms significantly decreased, including *suicide note, suicidal thoughts,* and *suicidal ideation*, translating into approximately 245 000, 155 000, and 80 000 fewer searches than expected, respectively. The only search term that significantly increased was potentially

associated with interest in suicide facts: *how many people commit suicide* (approximately 13 000 more searches than expected).

Women & Children

53. Saliva Viral Load Better Correlates with Clinical and Immunological Profiles in Children with Coronavirus Disease 2019. Chua GT, Wong JS, To KK, et al. *Emerg Microbes Infect.* 2021 Jan 19:1-25. doi: 10.1080/22221751.2021.1878937.

https://www.tandfonline.com/doi/full/10.1080/22221751.2021.1878937

FINDINGS: 91 patients were included between March and August 2020. NPS and saliva viral loads were correlated. Symptomatic patients had significantly higher NPS and saliva viral loads than asymptomatic patients. Serial NPS and saliva viral load measurements showed that the log10 NPS and saliva viral loads for all patients were inversely correlated with the days from symptom onset with statistical significance. Patients with cough, sputum, and headache had significantly higher saliva, but not NPS, viral loads. Higher saliva, but not NPS, viral loads were associated with total lymphopenia, CD3 and CD4 lymphopenia, and were inversely correlated with total lymphocyte, CD3, CD4, CD8, B, and NK lymphocyte counts. Interpretation: Saliva viral loads on admission in children correlated better with clinical and immunological profiles than NPS.

54. Prevalence of SARS-CoV-2 Infection in Children and Their Parents in Southwest Germany.

Tönshoff B, Müller B, Elling R, et al. *JAMA Pediatr*. 2021 Jan 22. doi: 10.1001/jamapediatrics.2021.0001.

https://jamanetwork.com/journals/jamapediatrics/fullarticle/2775656

Findings: This study included 4964 participants: 2482 children (median age, 6 years; 1265 boys [51.0%]) and 2482 parents (median age, 40 years; 615 men [24.8%]). Two participants (0.04%) tested positive for SARS-CoV-2 RNA. The estimated SARS-CoV-2 seroprevalence was low in parents (1.8% [95% CI, 1.2-2.4%]) and 3-fold lower in children (0.6% [95% CI, 0.3-1.0%]). Among 56 families with at least 1 child or parent with seropositivity, the combination of a parent with seropositivity and a corresponding child with seronegativity was 4.3 (95% CI, 1.19-15.52) times higher than the combination of a parent who was seronegative and a corresponding child with seropositivity. We observed virus-neutralizing activity for 66 of 70 IgG-positive serum samples (94.3%). In this cross-sectional study, the spread of SARS-CoV-2 infection during a period of lockdown in southwest Germany was particularly low in children aged 1 to 10 years. Accordingly, it is unlikely that children have boosted the pandemic. This SARS-CoV-2 prevalence study, which appears to be the largest focusing on children, is instructive for how ad hoc mass testing provides the basis for rational political decision-making in a pandemic.

55. Neonates Born to Mothers with COVID-19: Data from the Spanish Society of Neonatology Registry. Sánchez-Luna M, Fernández Colomer B, de Alba Romero C, et al. *Pediatrics*. 2021 Jan 21:e2020015065. doi: 10.1542/peds.2020-015065.

https://pediatrics.aappublications.org/content/early/2021/01/19/peds.2020-015065

Findings: Between March 8, 2020, and May 26, 2020, the data of 503 neonates born to 497 mothers diagnosed with COVID-19 during pregnancy or at the time of delivery were collected

by 79 hospitals throughout Spain. The rate of preterm deliveries was 15.7% and of cesarean deliveries, 33%. The most common diagnostic test was detection of viral RNA by polymerase chain reaction of nasopharyngeal swabs at a median age of 3 hours after delivery (1-12 hours). Almost one-half of neonates were left skin-to-skin after delivery, and delayed clamping of umbilical cords was performed in 43% of neonates. Also, 62.3% of asymptomatic neonates were managed with rooming-in. Maternal milk was received by 76.5% of neonates, 204 of them as exclusive breastfeeding. The current study indicates that there is no need for separation of mothers from neonates, allowing delayed cord clamping and skin-to-skin contact along with maintenance of breastfeeding in a high percentage of newborns from mothers with COVID-19.

56. Pregnancy as a risk factor for severe coronavirus 2019 (COVID-19) disease using standardized clinical criteria. Oakes MC, Kernberg AS, Carter EB, et al. *Am J Obstet Gynecol MFM*. 2021 Jan 22:100319. doi: 10.1016/j.ajogmf.2021.100319.

https://www.sciencedirect.com/science/article/pii/S2589933321000148?via%3Dihub Findings: This is a retrospective cohort study of women aged 13-45 years and diagnosed with symptomatic COVID-19 between May 28-July 22, 2020. Of 262 women aged 13-45 years with symptomatic COVID-19, 22 (8.4%) were pregnant and 240 (91.6%) were non-pregnant. After adjusting for covariates potentially associated with the primary outcome, symptomatic pregnant women were at significantly increased risk for severe COVID-19 compared to nonpregnant women using both the World Health Organization Ordinal Scale for Clinical Improvement and Novel Coronavirus Pneumonia Emergency Response Epidemiology Team criteria. Pregnancy significantly increases the risk for severe COVID-19 as defined by nonadmission based, clinical criteria.

GUIDELINES & CONSENSUS STATEMENTS

NATIONAL STRATEGY FOR THE COVID-19 RESPONSE AND PANDEMIC PREPAREDNESS

The NICE COVID-19 rapid guideline on haematopoietic stem cell transplantation: development, implementation and impact. Orchard K, Dignan FL, Lee J, et al. *Br J Haematol*. 2021 Jan 20. doi: 10.1111/bjh.17280.

SARS-CoV-2 vaccination for patients with inflammatory bowel diseases: recommendations from an international consensus meeting. International Organization for the Study of Inflammatory Bowel Diseases (IOIBD). *Gut*. 2021 Jan 20:gutjnl-2020-324000. doi: 10.1136/gutjnl-2020-324000.

The Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19: Molecular Diagnostic Testing. Hanson KE, Caliendo AM, Arias CA, et al. *Clin Infect Dis*. 2021 Jan 22:ciab048. doi: 10.1093/cid/ciab048.

Managing the long term effects of covid-19: summary of NICE, SIGN, and RCGP rapid guideline. Shah W, Hillman T, Playford ED, Hishmeh L. *BMJ.* 2021 Jan 22;372:n136. doi: 10.1136/bmj.n136.

FDA / CDC / NIH / WHO Updates

CDC - Interim Clinical Considerations for Use of mRNA COVID-19 Vaccines Currently Authorized in the United States

UK New and Emerging Respiratory Virus Threats Advisory Group - NERVTAG note on B.1.1.7 severity

CDC - US COVID-19 Cases Caused by Variants

Commentary & News

Moderna COVID-19 Vaccine Retains Neutralizing Activity Against Emerging Variants First Identified in the U.K. and the Republic of South Africa **see associated Preprint article above under Vaccine section

PFIZER AND BIONTECH PUBLISH RESULTS OF STUDY SHOWING COVID-19 VACCINE ELICITS ANTIBODIES THAT NEUTRALIZE PSEUDOVIRUS BEARING THE SARS-COV-2 U.K. STRAIN SPIKE PROTEIN IN CELL CULTURE **see associated Preprint article above under Vaccine section

Executive Order on Protecting the Federal Workforce and Requiring Mask-Wearing

Executive Order on Organizing and Mobilizing the United States Government to Provide a Unified and Effective Response to Combat COVID-19 and to Provide United States Leadership on Global Health and Security

New California Variant May Be Driving Virus Surge There, Study Suggests

California State Epidemiologist Issues Update on Moderna COVID-19 Vaccine

<u>Lilly's neutralizing antibody bamlanivimab (LY-CoV555) prevented COVID-19 at nursing homes in the</u> <u>BLAZE-2 trial, reducing risk by up to 80 percent for residents</u>

Why Vaccines Alone Will Not End the Pandemic

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