

COVID-19 Resource Desk

#42 | 2.3.2021 to 2.9.2021

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New Research

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Basic Science / Virology / Pre-clinical

- 1. A Novel DNA and Protein Combination COVID-19 Vaccine Formulation Provides Full Protection against SARS-CoV-2 in Rhesus Macaques.** Li Y, Bi Y, Xiao H, et al. *Emerg Microbes Infect.* 2021 Feb 8:1-19. doi: 10.1080/22221751.2021.1887767.
<https://www.tandfonline.com/doi/full/10.1080/22221751.2021.1887767>
Findings: The current study aims to develop a safe and highly immunogenic COVID-19 vaccine. The novel combination of a DNA vaccine encoding the full-length Spike (S) protein of SARS-CoV-2 and a recombinant S1 protein vaccine induced high level neutralizing antibody and T cell immune responses in both small and large animal models. More significantly, the co-delivery of DNA and protein components at the same time elicited full protection against intratracheal challenge of SARS-CoV-2 viruses in immunized rhesus macaques. As both DNA and protein vaccines have been proven safe in previous human studies, and DNA vaccines are capable of eliciting germinal center B cell development, which is critical for high -affinity memory B cell responses, the DNA and protein co-delivery vaccine approach has great potential to serve as a safe and effective approach to develop COVID-19 vaccines that provide long-term protection.

Clinical Syndrome

- 2. Clinical characteristics and risk factors for symptomatic venous thromboembolism in hospitalized COVID-19 patients: A multicenter retrospective study.** Thrombo-COVID-19 Collaborative. *J Thromb Haemost.* 2021 Feb 3. doi: 10.1111/jth.15261.
<https://onlinelibrary.wiley.com/doi/abs/10.1111/jth.15261>
Findings: This retrospective study enrolled all COVID-19 patients with a subsequent VTE in 16 centers in China from January 1 to March 31, 2020. A total of 2779 patients were confirmed with COVID-19. In comparison with 23,434 non-COVID-19 medical inpatients, the ORs for developing symptomatic VTE in severe and non-severe hospitalized COVID-19 patients were 5.94 and 2.79, respectively. When 104 VTE cases and 208 Non-VTE cases were compared, pulmonary embolism cases had a higher rate for in-hospital death. VTE developed at a median of 21 days since onset. Independent factors for VTE were advancing age, cancer, longer interval from symptom onset to admission, lower fibrinogen and higher D-dimer on admission, and D-dimer increment (DI) ≥ 1.5 fold; of these, DI ≥ 1.5 fold had the most significant association (OR

14.18, 95%CI 6.25-32.18, $P = 2.23 \times 10^{-10}$). A novel model consisting of simple 3 coagulation variables (fibrinogen and D-dimer levels on admission, and $DI \geq 1.5$ fold) showed good prediction for symptomatic VTE. There is an excess risk of VTE in hospitalized COVID-19 patients. The novel model can help early identification of patients who are at high risk for VTE.

3. **COVID-19-Associated Pulmonary Aspergillosis, March-August 2020.** FungiScope European Confederation of Medical Mycology/The International Society for Human and Animal Mycology Working Group. *Emerg Infect Dis.* 2021 Feb 4;27(4). doi: 10.3201/eid2704.204895.

https://wwwnc.cdc.gov/eid/article/27/4/20-4895_article

Findings: We collected data from 186 patients who had coronavirus disease-associated pulmonary aspergillosis (CAPA) worldwide during March-August 2020. Overall, 182 patients were admitted to the intensive care unit (ICU), including 180 with acute respiratory distress syndrome and 175 who received mechanical ventilation. CAPA was diagnosed a median of 10 days after coronavirus disease diagnosis. *Aspergillus fumigatus* was identified in 80.3% of patient cultures, 4 of which were azole-resistant. Most (52.7%) patients received voriconazole. In total, 52.2% of patients died; of the deaths, 33.0% were attributed to CAPA. We found that the cumulative incidence of CAPA in the ICU ranged from 1.0% to 39.1%.

4. **COVID-19 versus Non-COVID ARDS: Comparison of Demographics, Physiologic Parameters, Inflammatory Biomarkers and Clinical Outcomes.** Bain W, Yang H, Shah FA, et al. *Ann Am Thorac Soc.* 2021 Feb 5. doi: 10.1513/AnnalsATS.202008-1026OC.

<https://www.atsjournals.org/doi/10.1513/AnnalsATS.202008-1026OC>

Findings: We enrolled 27 patients with COVID-19 ARDS in a prospective, observational cohort study, and compared them with a historical, pre-COVID-19 cohort of patients with viral ARDS (n=14), bacterial ARDS (n=21), and ARDS due to culture-negative pneumonia (n=30). Patients with COVID-19 ARDS had higher body mass index and were more likely to be Black, or residents of skilled nursing facilities, compared to non-COVID-19 ARDS. COVID-19 patients had lower delivered minute ventilation compared to bacterial and culture-negative ARDS, but not compared to viral ARDS. We found no differences in static compliance, hypoxemic indices or carbon dioxide clearance between groups. COVID-19 patients had lower IL-6 levels compared to bacterial and culture-negative ARDS at early time points post-intubation, but no differences in IL-6 levels compared to viral ARDS. COVID-19 patients had longer duration of mechanical ventilation but similar 60-day mortality, both in unadjusted and adjusted analyses. COVID-19 ARDS bears several similarities to viral ARDS but demonstrates lower minute ventilation and lower systemic levels of IL-6 compared to bacterial and culture-negative ARDS. COVID-19 ARDS was associated with longer dependence on mechanical ventilation compared to non-COVID ARDS. Such detectable differences of COVID-19 do not merit deviation from evidence-based management of ARDS but suggest priorities for clinical research to better characterize and treat this new clinical entity.

5. **Incidence and Prognosis of Ventilator-Associated Pneumonia in Critically Ill Patients with COVID-19: A Multicenter Study.** Giacobbe DR, Battaglini D, Enrile EM, et al. *J Clin Med.* 2021 Feb 3;10(4):555. doi: 10.3390/jcm10040555. <https://www.mdpi.com/2077-0383/10/4/555>

Findings: From 15 February to 15 May 2020, 586 COVID-19 patients were admitted to the participating ICU. Of them, 171 developed VAP (29%) and were included in the study. The incidence rate of VAP was of 18 events per 1000 ventilator days. Deep respiratory cultures were available and positive in 77/171 patients (45%). The most frequent organisms were *Pseudomonas aeruginosa* (27/77, 35%) and *Staphylococcus aureus* (18/77, 23%). The 30-day case-fatality of VAP was 46% (78/171). In multivariable analysis, septic shock at VAP onset and acute respiratory distress syndrome at VAP onset were associated with fatality. In conclusion, VAP is frequent in critically ill COVID-19 patients. The related high fatality is likely the sum of the unfavorable prognostic impacts of the underlying viral and the superimposed bacterial diseases.

Diagnosics & Screening

6. **Performance of Oropharyngeal Swab Testing Compared with Nasopharyngeal Swab Testing for Diagnosis of Coronavirus Disease 2019-United States, January 2020-February 2020.** Patel MR, Carroll D, Ussery E, et al. *Clin Infect Dis*. 2021 Feb 1;72(3):403-410. doi: 10.1093/cid/ciaa759. <https://academic.oup.com/cid/article/72/3/482/5858273>
Findings: Among 146 nasopharyngeal (NP) and oropharyngeal (OP) swab pairs collected ≤7 days after illness onset, Real-Time Reverse Transcriptase Polymerase Chain Reaction assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 RT-PCR) diagnostic results were 95.2% concordant. However, NP swab cycle threshold values were lower (indicating more virus) in 66.7% of concordant-positive pairs, suggesting NP swabs may more accurately detect the amount of SARS-CoV-2.
7. **Sensitivity of anti-SARS-CoV-2 serological assays in a high-prevalence setting.** Müller L, Ostermann PN, Walker A, et al. *Eur J Clin Microbiol Infect Dis*. 2021 Feb 3:1-9. doi: 10.1007/s10096-021-04169-7. <https://link.springer.com/article/10.1007/s10096-021-04169-7>
Findings: The aim of this study was to assess four commercial serological tests from EUROIMMUN, DiaSorin, Abbott, and Roche as well as an in-house immunofluorescence and neutralization test for their capability to identify SARS-CoV-2 seropositive individuals in a high-prevalence setting. Therefore, 42 social and working contacts of a German super-spreader were tested. Consistent with a high-prevalence setting, 26 of 42 were SARS-CoV-2 seropositive by neutralization test (NT), and immunofluorescence test (IFT) confirmed 23 of these 26 positive test results (NT 61.9% and IFT 54.8% seroprevalence). Four commercial assays detected anti-SARS-CoV-2 antibodies in 33.3-40.5% individuals. Besides an overall discrepancy between the NT and the commercial assays regarding their sensitivity, this study revealed that commercial SARS-CoV-2 spike-based assays are better to predict the neutralization titer than nucleoprotein-based assays are.
8. **Comparative cost-effectiveness of SARS-CoV-2 testing strategies in the USA: a modelling study.** Du Z et al. *Lancet Public Health* 2021 Feb 4. DOI:[https://doi.org/10.1016/S2468-2667\(21\)00002-5](https://doi.org/10.1016/S2468-2667(21)00002-5) [https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667\(21\)00002-5/fulltext](https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(21)00002-5/fulltext)

Findings: We used a multiscale model that incorporates SARS-CoV-2 transmission at the population level and daily viral load dynamics at the individual level to assess eight surveillance testing strategies that varied by testing frequency (from daily to monthly testing) and isolation period (1 or 2 weeks), compared with the status-quo strategy of symptom-based testing and isolation. Our modelling showed that daily testing combined with a 2-week isolation period was the most costly strategy considered, reflecting increased costs with greater test frequency and length of isolation period. Assuming a societal willingness to pay of US\$100 000 per YLL averted and a price of \$5 per test, the strategy most likely to be cost-effective under a rapid transmission scenario (R_e of 2.2) is weekly testing followed by a 2-week isolation period subsequent to a positive test result. Under low transmission scenarios (R_e of 1.2), monthly testing of the population followed by 1-week isolation rather than 2-week isolation is likely to be most cost-effective. Expanded surveillance testing is more likely to be cost-effective than the status-quo testing strategy if the price per test is less than \$75 across all transmission rates considered. Extensive expansion of SARS-CoV-2 testing programmes with more frequent and rapid tests across communities coupled with isolation of individuals with confirmed infection is essential for mitigating the COVID-19 pandemic. Furthermore, resources recouped from shortened isolation duration could be cost-effectively allocated to more frequent testing.

Epidemiology & Public Health

9. **Trends in US Emergency Department Visits for Mental Health, Overdose, and Violence Outcomes Before and During the COVID-19 Pandemic.** Holland KM, Jones C, Vivolo-Kantor AM, et al. *JAMA Psychiatry*. 2021 Feb 3. doi: 10.1001/jamapsychiatry.2020.4402. <https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2775991>
Findings: This cross-sectional study used data from the CDC's National Syndromic Surveillance Program to examine national changes in ED visits for MHCs, SAs, ODs, and violence from December 30, 2018, to October 10, 2020 (before and during the COVID-19 pandemic). When the median ED visit counts between March 15 and October 10, 2020, were compared with the same period in 2019, the 2020 counts were significantly higher for SAs ($n = 4940$ vs 4656 , $P = .02$), all ODs ($n = 15\,604$ vs $13\,371$, $P < .001$), and opioid ODs ($n = 5502$ vs 4168 , $P < .001$); counts were significantly lower for IPV ED visits ($n = 442$ vs 484 , $P < .001$) and SCAN ED visits ($n = 884$ vs 1038 , $P < .001$). These findings suggest that ED care seeking shifts during a pandemic, underscoring the need to integrate mental health, substance use, and violence screening and prevention services into response activities during public health crises.

10. **The Impact of State Mask-Wearing Requirements on the Growth of COVID-19 Cases in the United States.** Rebeiro PF, Aronoff DM, Smith MK. *Clin Infect Dis*. 2021 Feb 7:ciab101. doi: 10.1093/cid/ciab101. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab101/6129930>
Findings: In our ecologic analysis of US states, piecewise multivariable models showed lower post- vs. pre-mask case-rate slopes, with -1.08% per 100,000 per day among early- and -0.37% per 100,000 per day among late- versus never-adopter states. Our findings support statewide mask requirements to mitigate COVID-19 transmission.

- 11. Decline in COVID-19 Hospitalization Growth Rates Associated with Statewide Mask Mandates — 10 States, March–October 2020.** Joo H, Miller GF, Sunshine G, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 5 February 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7006e2>
Findings: During March 22–October 17, 2020, 10 sites participating in the COVID-19–Associated Hospitalization Surveillance Network in states with statewide mask mandates reported a decline in weekly COVID-19–associated hospitalization growth rates by up to 5.5 percentage points for adults aged 18–64 years after mandate implementation, compared with growth rates during the 4 weeks preceding implementation of the mandate. Mask-wearing is a component of a multipronged strategy to decrease exposure to and transmission of SARS-CoV-2 and reduce strain on the health care system, with likely direct effects on COVID-19 morbidity and associated mortality.
- 12. Cardiac arrest in COVID-19: characteristics and outcomes of in- and out-of-hospital cardiac arrest. A report from the Swedish Registry for Cardiopulmonary Resuscitation.** Sultanian P, Lundgren P, Strömsöe A, et al. *Eur Heart J*. 2021 Feb 5:ehaa1067. doi: 10.1093/eurheartj/ehaa1067. <https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaa1067/6128749>
Findings: We included all patients reported to the Swedish Registry for Cardiopulmonary Resuscitation from 1 January to 20 July 2020. We defined 16 March 2020 as the start of the pandemic. We studied 1946 cases of OHCA and 1080 cases of IHCA during the entire period. During the pandemic, 88 (10.0%) of OHCA and 72 (16.1%) of IHCA had ongoing COVID-19. With regards to OHCA during the pandemic, the odds ratio for 30-day mortality in COVID-19-positive cases, compared with COVID-19-negative cases, was 3.40; the corresponding hazard ratio was 1.45. Adjusted 30-day survival was 4.7% for patients with COVID-19, 9.8% for patients without COVID-19, and 7.6% in the pre-pandemic period. With regards to IHCA during the pandemic, the odds ratio for COVID-19-positive cases, compared with COVID-19-negative cases, was 2.27; the corresponding hazard ratio was 1.48. Adjusted 30-day survival was 23.1% in COVID-19-positive cases, 39.5% in patients without COVID-19, and 36.4% in the pre-pandemic period. During the pandemic phase, COVID-19 was involved in at least 10% of all OHCA and 16% of IHCA, and, among COVID-19 cases, 30-day mortality was increased 3.4-fold in OHCA and 2.3-fold in IHCA.
- 13. Genomic epidemiology identifies emergence and rapid transmission of SARS-CoV-2 B.1.1.7 in the United States.** Washington NL et al. *medRxiv PREPRINT*. 2021.02.06.21251159; doi: <https://doi.org/10.1101/2021.02.06.21251159>
Findings: As of January of 2021, the highly transmissible B.1.1.7 variant of SARS-CoV-2, which was first identified in the United Kingdom (U.K.), has gained a strong foothold across the world. Because of the sudden and rapid rise of B.1.1.7, we investigated the prevalence and growth dynamics of this variant in the United States (U.S.), tracking it back to its early emergence and onward local transmission. We found that the RT-qPCR testing anomaly of S gene target failure (SGTF), first observed in the U.K., was a reliable proxy for B.1.1.7 detection. We sequenced 212 B.1.1.7 SARS-CoV-2 genomes collected from testing facilities in the U.S. from December 2020 to January 2021. We found that while the fraction of B.1.1.7 among SGTF samples varied by state, detection of the variant increased at a logistic rate similar to those observed elsewhere, with a

doubling rate of a little over a week and an increased transmission rate of 35-45%. By performing time-aware Bayesian phylodynamic analyses, we revealed several independent introductions of B.1.1.7 into the U.S. as early as late November 2020, with onward community transmission enabling the variant to spread to at least 30 states as of January 2021. Our study shows that the U.S. is on a similar trajectory as other countries where B.1.1.7 rapidly became the dominant SARS-CoV-2 variant, requiring immediate and decisive action to minimize COVID-19 morbidity and mortality.

14. **COVID-19 and dementia: Analyses of risk, disparity, and outcomes from electronic health records in the US.** Wang Q, Davis PB, Gurney ME, et al. *Alzheimer's & Dementia*. 09 February 2021 <https://doi.org/10.1002/alz.12296>
Findings: Patients with dementia were at increased risk for COVID-19 compared to patients without dementia, with the strongest effect for vascular dementia, followed by presenile dementia, Alzheimer's disease, senile dementia and post-traumatic dementia. Blacks with dementia had higher risk of COVID-19 than Whites. The 6-month mortality and hospitalization risks in patients with dementia and COVID-19 were 20.99% and 59.26%, respectively.

15. **Racial Disparities in COVID-19 Testing and Outcomes: Retrospective Cohort Study in an Integrated Health System.** Escobar GJ, Adams AS, Liu VX, et al. *Ann Intern Med*. 2021 Feb 9. doi: 10.7326/M20-6979. <https://www.acpjournals.org/doi/10.7326/M20-6979>
Findings: Among 3 481 716 eligible members, 42.0% were White, 6.4% African American, 19.9% Hispanic, and 18.6% Asian; 13.0% were of other or unknown race. Of eligible members, 91 212 (2.6%) were tested for SARS-CoV-2 infection and 3686 had positive results (overall incidence, 105.9 per 100 000 persons; by racial group, White, 55.1; African American, 123.1; Hispanic, 219.6; Asian, 111.7; other/unknown, 79.3). African American persons had the highest unadjusted testing and mortality rates, White persons had the lowest testing rates, and those with other or unknown race had the lowest mortality rates. Compared with White persons, adjusted testing rates among non-White persons were marginally higher, but infection rates were significantly higher; adjusted odds ratios [aORs] for African American persons, Hispanic persons, Asian persons, and persons of other/unknown race were 2.01, 3.93, 2.19, and 1.57, respectively. Geographic analyses showed that infections clustered in areas with higher proportions of non-White persons. Compared with White persons, adjusted hospitalization rates for African American persons, Hispanic persons, Asian persons, and persons of other/unknown race were 1.47, 1.42, 1.47, and 1.03, respectively. Race was the most important predictor of SARS-CoV-2 infection. After infection, race was associated with increased hospitalization risk but not mortality.

Healthcare Delivery & Healthcare Workers

16. **COVID-19 Vaccine Acceptance among Health Care Workers in the United States.** Shekhar R, Sheikh AB, Upadhyay S, et al. *Vaccines*. 2021 Feb 3;9(2):119. doi: 10.3390/vaccines9020119. <https://www.mdpi.com/2076-393X/9/2/119>
Findings: We conducted a cross sectional study to assess the attitude of HCWs toward COVID-19 vaccination. Data were collected between 7 October and 9 November 2020. We received

4080 responses out of which 3479 were complete responses and were included in the final analysis. 36% of respondents were willing to take the vaccine as soon as it became available while 56% were not sure or would wait to review more data. Only 8% of HCWs do not plan to get vaccine. Vaccine acceptance increased with increasing age, education, and income level. A smaller percentage of female (31%), Black (19%), Latinx (30%), and rural (26%) HCWs were willing to take the vaccine as soon as it became available than the overall study population. Direct medical care providers had higher vaccine acceptance (49%). Safety (69%), effectiveness (69%), and speed of development/approval (74%) were noted as the most common concerns regarding COVID-19 vaccination in our survey.

17. Cross-sectional Assessment of COVID-19 Vaccine Acceptance Among Health Care Workers in Los Angeles. Gadoth A, Halbrook M, Martin-Blais R, et al. *Ann Intern Med.* 2021 Feb 9. doi: 10.7326/M20-7580. <https://www.acpjournals.org/doi/10.7326/M20-7580>

Findings: In total, 609 enrollees completed the optional questionnaire; complete-case analysis resulted in an analytical sample of 540 survey participants. A majority of participants were female (71.7%), were White (57.0%), were aged 30 to 49 years (63.0%), and had an advanced degree (62.8%). Almost all respondents held jobs with direct patient contact (85.4%). Most participants (65.5%) indicated they would delay vaccination once coronavirus vaccines became available for distribution (49.4% would prefer to wait and see how the vaccine affects others first, and 16.1% would not get it soon but indicated they might in the future), and 1.30% never intend to get vaccinated. Compared with prescribing clinicians, other HCWs were about 20% to 30% more likely to delay or decline a coronavirus vaccine when all other demographic factors were held equal. Participants identifying as Asian (23.9%) or Latino (26.2%) were less likely to accept vaccination immediately upon availability compared with those in other racial and ethnic groups. Health care workers aged 50 years or older were more likely than their younger coworkers to accept vaccination right away.

18. Coronavirus Disease 2019 Immediately Increases Burnout Symptoms in ICU Professionals: A Longitudinal Cohort Study. Kok N, van Gorp J, Teerenstra S, et al. *Crit Care Med.* 2021 Jan 28. doi: 10.1097/CCM.0000000000004865.

Findings: Caregivers from five ICUs based in a single university medical center plus another adult ICU based on a separate teaching hospital in the Netherlands were sent a baseline survey in October-December 2019 (252 respondents, response rate: 53%), and a follow-up survey was sent in May-June 2020 (233 respondents, response rate: 50%). Burnout symptoms and moral distress measured with the Maslach Burnout Inventory and the Moral Distress Scale, respectively. The prevalence of burnout symptoms was 23.0% before coronavirus disease 2019 and 36.1% at postpeak time, with higher rates in nurses (38.0%) than in physicians (28.6%). Reversely, the incidence rate of new burnout cases among physicians was higher (26.7%) than nurses (21.9%). Higher prevalence of burnout symptoms was observed in the postpeak coronavirus disease 2019 period, for nurses, for professionals working overtime, and for professionals directly engaged with care for coronavirus disease 2019 patients (odds ratio, 1.87; 95% CI, 1.35-2.60). Physicians were more likely than nurses to develop burnout symptoms due to coronavirus disease 2019. This study shows that overburdening of ICU professionals during an extended period of time leads to symptoms of burnout. Working long hours and under

conditions of scarcity of staff, time, and resources comes at the prize of ICU professionals' mental health.

Laboratory Results

19. **Dynamics of Neutralizing Antibody Titers in the Months after Severe Acute Respiratory Syndrome Coronavirus 2 Infection.** Crawford KHD, Dingens AS, Eguia R, et al. *J Infect Dis.* 2021 Feb 3;223(2):197-205. doi: 10.1093/infdis/jiaa618. <https://academic.oup.com/jid/article/223/2/197/5916372>
Findings: In this study, we quantified how levels of these antibodies change in the months after SARS-CoV-2 infection by examining longitudinal samples collected approximately 30-152 days after symptom onset from a prospective cohort of 32 recovered individuals with asymptomatic, mild, or moderate-severe disease. Neutralizing antibody titers declined an average of about 4-fold from 1 to 4 months after symptom onset. This decline in neutralizing antibody titers was accompanied by a decline in total antibodies capable of binding the viral spike protein or its receptor-binding domain. Importantly, our data are consistent with the expected early immune response to viral infection, where an initial peak in antibody levels is followed by a decline to a lower plateau.
20. **Inflammatory cytokine patterns associated with neurological diseases in COVID-19.** Espíndola OM, Gomes YCP, Brandão CO, et al. *Ann Neurol.* 2021 Feb 6. doi: 10.1002/ana.26041. <https://onlinelibrary.wiley.com/doi/10.1002/ana.26041>
Findings: Patients with COVID-19 can present with distinct neurological manifestations. This study shows that inflammatory neurological diseases were associated with increased levels of IL-2, IL-4, IL-6, IL-10, IL-12, CXCL8, and CXCL10 in the cerebrospinal fluid (CSF). Conversely, encephalopathy was associated with high serum levels of IL-6, CXCL8, and active TGF- β 1. Inflammatory syndromes of the central nervous system (CNS) in COVID-19 can appear early, as a para-infectious process without significant systemic involvement, or without direct evidence of SARS-CoV-2 neuroinvasion. At the same time, encephalopathy is mainly influenced by peripheral events, including inflammatory cytokines.

Prognosis

21. **Use of Dipeptidyl Peptidase-4 inhibitors and prognosis of COVID-19 in hospitalized patients with type 2 diabetes: a propensity score analysis from the CORONADO study.** CORONADO investigators. *Diabetes Obes Metab.* 2021 Feb 2. doi: 10.1111/dom.14324. <https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.14324>
Findings: 596 participants were under DPP-4 inhibitors before admission to hospital (24.3%). The primary outcome occurred at similar rates in users and non-users of DPP-4 inhibitors (27.7% vs 28.6%, P=0.68). In propensity analysis, the IPTW-adjusted models showed no significant association between use of DPP-4 inhibitors and the primary outcome within day 7 or day 28. Similar neutral findings were found between use of DPP-4 inhibitors and the risk of tracheal intubation and death. These data support the safety of DPP-4 inhibitors for diabetes management during the COVID-19 pandemic and they should not be discontinued.

22. Relation of Cardiovascular Risk Factors to Mortality and Cardiovascular Events in Hospitalized Patients with Coronavirus Disease 2019 (From the Yale COVID-19 Cardiovascular Registry).

Pareek M, Singh A, Vadlamani L, et al. *Am J Cardiol.* 2021 Feb 1:S0002-9149(21)00100-4. doi: 10.1016/j.amjcard.2021.01.029.

<https://www.sciencedirect.com/science/article/pii/S0002914921001004>

Findings: We conducted a prospective cohort study at a tertiary care center to identify risk factors for in-hospital mortality and major adverse cardiovascular events (MACE; a composite of myocardial infarction, stroke, new acute decompensated heart failure, venous thromboembolism, ventricular or atrial arrhythmia, pericardial effusion, or aborted cardiac arrest) among consecutively hospitalized adults with COVID-19. The study population comprised 586 COVID-19 positive patients. After adjustment for demographics, presentation, and laboratory findings, predictors of MACE were higher respiratory rates, altered mental status, and laboratory abnormalities, including higher troponin T ($p < 0.05$). In conclusion, poor prognostic markers among hospitalized patients with COVID-19 included older age, pre-existing cardiovascular disease, respiratory failure, altered mental status, and higher troponin T concentrations.

23. Increased hazard of death in community-tested cases of SARS-CoV-2 Variant of Concern

202012/01. CMMID COVID-19 Working Group. *medRxiv PREPRINT.* 2021.02.01.21250959; doi: <https://doi.org/10.1101/2021.02.01.21250959>

<https://www.medrxiv.org/content/10.1101/2021.02.01.21250959v1>

Findings: VOC 202012/01, a SARS-CoV-2 variant first detected in the United Kingdom in September 2020, has spread to multiple countries worldwide. Several studies have established that this novel variant is more transmissible than preexisting variants of SARS-CoV-2, but have not identified whether the new variant leads to any change in disease severity. We analyse a large database of SARS-CoV-2 community test results and COVID-19 deaths for England, representing approximately 47% of all SARS-CoV-2 community tests and 7% of COVID-19 deaths in England from 1 September 2020 to 22 January 2021. Fortunately, these SARS-CoV-2 tests can identify VOC 202012/01 because mutations in this lineage prevent PCR amplification of the spike gene target (S gene target failure, SGTF). We estimate that the hazard of death among SGTF cases is 30% (95% CI 9–56%) higher than among non-SGTF cases after adjustment for age, sex, ethnicity, deprivation level, care home residence, local authority of residence and date of test. In absolute terms, this increased hazard of death corresponds to the risk of death for a male aged 55–69 increasing from 0.56% to 0.73% (95% CI 0.60–0.86%) over the 28 days following a positive SARS-CoV-2 test in the community. Correcting for misclassification of SGTF, we estimate a 35% (12–64%) higher hazard of death associated with VOC 202012/01. Our analysis suggests that VOC 202012/01 is not only more transmissible than preexisting SARS-CoV-2 variants but may also cause more severe illness.

24. Effect of antitumor therapy on cancer patients infected by SARS-CoV-2: A systematic review and meta-analysis.

Li P, Li L, Wang S, et al. *Cancer Med.* 2021 Feb 6. doi: 10.1002/cam4.3754.

<https://onlinelibrary.wiley.com/doi/10.1002/cam4.3754>

Findings: For cancer patients with COVID-19, the death events related to antitumor treatment were higher than those with no antitumor treatment (OR = 1.55; 95% CI 1.07-2.25; $p = 0.021$). Compared with patients in the survival group, the non-survival group showed no significant differences in patients who received antitumor therapy. Compared with patients in the non-severe group, the severe group was more likely to receive antitumor therapy (OR = 1.50; 95% CI 1.02-2.19; $p = 0.037$) and there was a significant difference. The incidence of severe events was higher in the subgroup of chemotherapy (OR = 1.73; 95% CI 1.09-2.73). The synthesized evidence suggests that cancer patients with COVID-19 who received antitumor treatment shortly before symptom onset are more likely to experience severe symptoms and have high mortality. Receiving chemotherapy is an unfavorable factor for the prognosis of cancer patients with COVID-19.

25. **Validating the RISE UP score for predicting prognosis in patients with COVID-19 in the emergency department: a retrospective study.** van Dam PM, Zelis N, Stassen P, et al. *BMJ Open*. 2021 Feb 5;11(2):e045141. doi: 10.1136/bmjopen-2020-045141.

<https://bmjopen.bmj.com/content/11/2/e045141.info>

Findings: Within 30 days after presentation, 167 patients (26.0%) died and 102 patients (15.9%) were admitted to ICU. The RISE UP score showed good discriminatory value for 30-day mortality and for the composite outcome. Patients with RISE UP scores below 10% ($n=121$) had favourable outcome (zero deaths and six ICU admissions), while those with scores above 30% ($n=221$) were at high risk of adverse outcome (46.6% mortality and 19.0% ICU admissions). The RISE UP score is an accurate prognostic model for adverse outcome in ED patients with COVID-19. It can be used to identify patients at risk of short-term adverse outcome and may help guide decision-making and allocating healthcare resources.

26. **SARS-CoV-2 infection in acute pancreatitis increases disease severity and 30-day mortality: COVID PAN collaborative study.** Pandanaboyana S, Moir J, Leeds JS, et al. *Gut*. 2021 Feb 5;gutjnl-2020-323364. doi: 10.1136/gutjnl-2020-323364.

<https://gut.bmj.com/content/early/2021/02/05/gutjnl-2020-323364>

Findings: 1777 patients with AP were included during the study period from 1 March to 23 July 2020. 149 patients (8.3%) had concomitant SARS-CoV-2 infection. Overall, SARS-CoV-2-positive patients were older male patients and more likely to develop severe AP and ARDS. Unadjusted analysis showed that SARS-CoV-2-positive patients with AP were more likely to require ICU admission, local complications, persistent organ failure, prolonged hospital stay and a higher 30-day mortality. Adjusted analysis showed length of stay, persistent organ failure and 30-day mortality were significantly higher in SARS-CoV-2 co-infection. Patients with AP and coexistent SARS-CoV-2 infection are at increased risk of severe AP, worse clinical outcomes, prolonged length of hospital stay and high 30-day mortality.

27. **Age and frailty are independently associated with increased COVID-19 mortality and increased care needs in survivors: results of an international multi-centre study.** Geriatric Medicine Research Collaborative. *Age Ageing*. 2021 Feb 5:afab026. doi:

10.1093/ageing/afab026. <https://academic.oup.com/ageing/advance-article/doi/10.1093/ageing/afab026/6128535>

Findings: Data from 5,711 patients from 55 hospitals in 12 countries were included (median age 74, 55.2% male). The risk of death increased independently with increasing age (>80 vs 18-49: HR 3.57, CI 2.54-5.02), frailty (CFS 8 vs 1-3: HR 3.03, CI 2.29-4.00) inflammation, renal disease, cardiovascular disease, and cancer, but not delirium. Age, frailty, delirium, dementia, and mental health diagnoses were all associated with increased risk of higher care needs on discharge. The likelihood of adverse outcomes increased across all grades of CFS from 4 to 9. Age and frailty are independently associated with adverse outcomes in COVID-19. Risk of increased care needs was also increased in survivors of COVID-19 with frailty or older age.

28. **Asthma and risk of infection, hospitalisation, ICU admission and mortality from COVID-19: Systematic review and meta-analysis.** Sunjaya AP, Allida SM, Di Tanna GL, Jenkins C. *J Asthma*. 2021 Feb 8:1-22. doi: 10.1080/02770903.2021.1888116.

<https://www.tandfonline.com/doi/full/10.1080/02770903.2021.1888116>

Findings: Fifty-seven studies with an overall sample size of 587,280 were included. The prevalence of asthma among those infected with COVID-19 was 7.46% (95% CI =6.25-8.67). Non-severe asthma was more common than severe asthma (9.61% vs. 4.13%). Pooled analysis showed a 14% risk ratio reduction in acquiring COVID-19 (95% CI =0.80-0.94; $p < 0.0001$) and 13% reduction in hospitalisation with COVID-19 (95% CI =0.77-0.99, $p = 0.03$) for people with asthma compared with those without. There was no significant difference in the combined risk of requiring admission to ICU and/or receiving mechanical ventilation for people with asthma (RR =0.87 95% CI =0.94-1.37; $p = 0.19$) and risk of death from COVID-19 (RR =0.87; 95% CI =0.68-1.10; $p = 0.25$). The findings from this study suggest that the prevalence of people with asthma among COVID-19 patients is similar to the global prevalence of asthma. The overall findings suggest that people with asthma have a lower risk than those without asthma for acquiring COVID-19 and have similar clinical outcomes.

Survivorship & Rehabilitation

29. **Short-term outpatient follow-up of COVID-19 patients: A multidisciplinary approach.** de Graaf MA, Antoni ML, Ter Kuile MM, et al. *EclinicalMedicine*. 2021 Jan 28:100731. doi: 10.1016/j.eclinm.2021.100731. [https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00011-0/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00011-0/fulltext)

Findings: We evaluated patients at our outpatient clinic 6 weeks after discharge. Eighty-one patients were included of whom 34 (41%) had been admitted to the ICU. New York Heart Association class II-III was present in 62% of the patients. Left ventricular function was normal in 78% of patients. ICU patients had a lower diffusion capacity (mean difference 12,5% $P = 0.01$), lower forced expiratory volume in one second and forced vital capacity (mean difference 14.9%; $P < 0.001$; 15.4%; $P < 0.001$; respectively). Risk of depression, anxiety and PTSD were 17%, 5% and 10% respectively and similar for both ICU and non-ICU patients. Overall, most patients suffered from functional limitations. Dyspnea on exertion was most frequently reported, possibly related to decreased DLCO. This could be caused by pulmonary fibrosis, which should be investigated in long-term follow-up. In addition, mechanical ventilation, deconditioning, or pulmonary embolism may play an important role.

30. **Do Patients with Covid-19 Benefit from Rehabilitation? Functional outcomes of the first 100 patients in a Covid-19 rehabilitation unit.** Covid Rehabilitation Study Group. *Arch Phys Med Rehabil.* 2021 Feb 3:S0003-9993(21)00134-9. doi: 10.1016/j.apmr.2021.01.069. [https://www.archives-pmr.org/article/S0003-9993\(21\)00134-9/pdf](https://www.archives-pmr.org/article/S0003-9993(21)00134-9/pdf)
Findings: Inpatient rehabilitation for Covid-19 patients was associated with substantial motor, respiratory and functional improvement, especially in severe cases, even though there remained mild persistent autonomy loss upon discharge. Following acute stages, Covid-19, primarily a respiratory disease, might convert into a motor impairment correlated with the time spent in intensive care.
31. **Is COVID-19 severity associated with anti-spike antibody duration? Data from the ARCOVID prospective observational study.** Borgonovo F, Passerini M, Piscaglia M, et al. *J Infect.* 2021 Feb 2:S0163-4453(21)00048-7. doi: 10.1016/j.jinf.2021.01.023. [https://www.journalofinfection.com/article/S0163-4453\(21\)00048-7/fulltext](https://www.journalofinfection.com/article/S0163-4453(21)00048-7/fulltext)
Findings: The vast majority of COVID-19 recovered patients maintained a detectable anti-S titre after 7 months from SARS-CoV-2 infection irrespectively of disease severity. Studies are urgently needed to clarify if subjects recovered from COVID-19 with an anti-S titre would gain additional benefit from COVID-19 vaccination.
32. **Health outcomes and economic burden of hospitalized COVID-19 patients in the United States.** Di Fusco M, Shea KM, Lin J, et al. *J Med Econ.* 2021 Feb 8:1. doi: 10.1080/13696998.2021.1886109. <https://www.tandfonline.com/doi/full/10.1080/13696998.2021.1886109>
Findings: Of the 173,942 hospitalized COVID-19 patients, median age was 63 years, 51.0% were male, and 48.5% were covered by Medicare. The most prevalent concomitant medical conditions were cardiovascular disease (73.5%), hypertension (64.8%), diabetes (40.7%), obesity (27.0%), and chronic kidney disease (24.2%). Approximately one-fifth (21.9%) of the hospitalized COVID-19 patients were admitted to the ICU and 16.9% received IMV; most patients (73.6%) did not require ICU admission or IMV, and 12.4% required both. The median hospital LOS was 5 days, in-hospital mortality was 13.6%, median hospital charges were \$43,986, and median hospital costs were \$12,046. Hospital LOS and in-hospital mortality increased with ICU and/or IMV usage and age; hospital charges and costs increased with ICU and/or IMV usage. Patients with both ICU and IMV usage had the longest median hospital LOS (15 days), highest in-hospital mortality (53.8%), and highest hospital charges (\$198,394) and hospital costs (\$54,402).

Therapeutics

33. **Extracorporeal membrane oxygenation in patients with severe respiratory failure from COVID-19.** STOP-COVID Investigators. *Intensive Care Med.* 2021 Feb 2. doi: 10.1007/s00134-020-06331-9. <https://link.springer.com/article/10.1007/s00134-020-06331-9>
Findings: Among the 190 patients treated with ECMO, the median age was 49 years (IQR 41-58), 137 (72.1%) were men, and the median PaO₂/FiO₂ prior to ECMO initiation was 72 (IQR 61-90). At 60 days, 63 patients (33.2%) had died, 94 (49.5%) were discharged, and 33 (17.4%)

remained hospitalized. Among the 1297 patients eligible for the target trial emulation, 45 of the 130 (34.6%) who received ECMO died, and 553 of the 1167 (47.4%) who did not receive ECMO died. In the primary analysis, patients who received ECMO had lower mortality than those who did not (HR 0.55; 95% CI 0.41-0.74). Results were similar in a secondary analysis limited to patients with PaO₂/FiO₂ < 80 (HR 0.55; 95% CI 0.40-0.77). In select patients with severe respiratory failure from COVID-19, ECMO may reduce mortality.

34. **Efficacy and tolerability of bevacizumab in patients with severe Covid-19.** Pang J, Xu F, Aondio G, et al. *Nat Commun.* 2021 Feb 5;12(1):814. doi: 10.1038/s41467-021-21085-8.

<https://www.nature.com/articles/s41467-021-21085-8>

Findings: From Feb 15 to April 5, 2020, we conducted a single-arm trial (NCT04275414) and recruited 26 patients from 2-centers (China and Italy) with severe Covid-19, with respiratory rate ≥ 30 times/min, oxygen saturation $\leq 93\%$ with ambient air, or partial arterial oxygen pressure to fraction of inspiration O₂ ratio (PaO₂/FiO₂) >100 mmHg and ≤ 300 mmHg, and diffuse pneumonia confirmed by chest imaging. Followed up for 28 days. Among these, bevacizumab plus standard care markedly improves the PaO₂/FiO₂ ratios at days 1 and 7. By day 28, 24 (92%) patients show improvement in oxygen-support status, 17 (65%) patients are discharged, and none show worsen oxygen-support status nor die. Significant reduction of lesion areas/ratios are shown in chest computed tomography (CT) or X-ray within 7 days. Of 14 patients with fever, body temperature normalizes within 72 h in 13 (93%) patients. Relative to comparable controls, bevacizumab shows clinical efficacy by improving oxygenation and shortening oxygen-support duration. *Our findings suggest bevacizumab plus standard care is highly beneficial for patients with severe Covid-19. Randomized controlled trial is warranted.*

35. **IL-1 Receptor Antagonist Anakinra in the Treatment of COVID-19 Acute Respiratory Distress Syndrome: A Retrospective, Observational Study.** Franzetti M, Forastieri A, Borsa N, et al. *J Immunol.* 2021 Feb 5;ji2001126. doi: 10.4049/jimmunol.2001126.

<https://www.jimmunol.org/content/jimmunol/early/2021/02/04/jimmunol.2001126.full.pdf>

Findings: In this study, COVID-19 ARDS patients admitted to the Azienda Socio Sanitaria Territoriale of Lecco, Italy, between March 5th to April 15th, 2020, and who had received anakinra off-label were retrospectively evaluated and compared with a cohort of matched controls who did not receive immunomodulatory treatment. The population consisted of 112 patients (56 treated with anakinra and 56 controls). Survival at day 28 was obtained in 69 patients (61.6%) and was significantly higher in anakinra-treated patients than in the controls (75.0 versus 48.2%, $p = 0.007$). When stratified by continuous positive airway pressure support at baseline, anakinra-treated patients' survival was also significant compared with the controls ($p = 0.008$). In conclusion, anakinra improved overall survival and invasive ventilation-free survival and was well tolerated in patients with ARDS associated with COVID-19.

36. **SARS-CoV-2 evolution during treatment of chronic infection.** Kemp SA, Collier DA, Datir RP, et al. *Nature.* 2021 Feb 5. doi: 10.1038/s41586-021-03291-y.

<https://www.nature.com/articles/s41586-021-03291-y>

Findings: Here we report chronic SARS-CoV-2 with reduced sensitivity to neutralising antibodies in an immune suppressed individual treated with convalescent plasma, generating whole

genome ultradeep sequences over 23 time points spanning 101 days. Little change was observed in the overall viral population structure following two courses of remdesivir over the first 57 days. However, following convalescent plasma therapy we observed large, dynamic virus population shifts, with the emergence of a dominant viral strain bearing D796H in S2 and Δ H69/ Δ V70 in the S1 N-terminal domain NTD of the Spike protein. As passively transferred serum antibodies diminished, viruses with the escape genotype diminished in frequency, before returning during a final, unsuccessful course of convalescent plasma. In vitro, the Spike escape double mutant bearing Δ H69/ Δ V70 and D796H conferred modestly decreased sensitivity to convalescent plasma, whilst maintaining infectivity similar to wild type. D796H appeared to be the main contributor to decreased susceptibility but incurred an infectivity defect. The Δ H69/ Δ V70 single mutant had two-fold higher infectivity compared to wild type, possibly compensating for the reduced infectivity of D796H. These data reveal strong selection on SARS-CoV-2 during convalescent plasma therapy associated with emergence of viral variants with evidence of reduced susceptibility to neutralising antibodies.

37. Efficacy of convalescent plasma therapy for COVID-19: A systematic review and meta-analysis. Vegivinti CTR, Pederson JM, Saravu K, et al. *J Clin Apher.* 2021 Feb 5. doi:

10.1002/jca.21881. <https://onlinelibrary.wiley.com/doi/10.1002/jca.21881>

Findings: We screened 859 studies that met the search criteria, performed full-text reviews of 56 articles, and identified 15 articles that fulfilled inclusion criteria for meta-analysis. The odds of mortality were significantly lower in the convalescent plasma group compared to the control group, although results from two key randomized controlled trials did not support the mortality benefit. The odds of clinical improvement were significantly higher in the convalescent plasma group compared to the control group. There was no difference in hospital length of stay between the convalescent plasma group and the control group (MD = -0.49 days). In all, these data indicate that a mortality benefit with convalescent plasma is unclear, although there remain benefits with convalescent plasma therapy for COVID-19.

38. Azithromycin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. RECOVERY Collaborative Group. *Lancet.* 2021 Feb 2:S0140-6736(21)00149-5. doi: 10.1016/S0140-6736(21)00149-5.

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00149-5/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00149-5/fulltext)

FINDINGS: Between April 7 and Nov 27, 2020, of 16 442 patients enrolled in the RECOVERY trial, 9433 (57%) were eligible and 7763 were included in the assessment of azithromycin. The mean age of these study participants was 65.3 years and approximately a third were women (2944 [38%] of 7763). 2582 patients were randomly allocated to receive azithromycin and 5181 patients were randomly allocated to usual care alone. Overall, 561 (22%) patients allocated to azithromycin and 1162 (22%) patients allocated to usual care died within 28 days (rate ratio 0.97, 95% CI 0.87-1.07; p=0.50). No significant difference was seen in duration of hospital stay (median 10 days vs 11 days) or the proportion of patients discharged from hospital alive within 28 days. Among those not on invasive mechanical ventilation at baseline, no significant difference was seen in the proportion meeting the composite endpoint of invasive mechanical ventilation or death. In patients admitted to hospital with COVID-19, azithromycin did not improve survival or other prespecified clinical outcomes. Azithromycin use in patients admitted

to hospital with COVID-19 should be restricted to patients in whom there is a clear antimicrobial indication.

39. **Beneficial effects of colchicine for moderate to severe COVID-19: a randomised, double-blinded, placebo-controlled clinical trial.** Lopes MI, Bonjorno LP, Giannini MC, et al. *RMD Open*. 2021 Feb;7(1):e001455. doi: 10.1136/rmdopen-2020-001455.

<https://rmdopen.bmj.com/content/7/1/e001455>

Findings: Seventy-two patients (36 for placebo and 36 for colchicine) completed the study. Median (and IQR) time of need for supplemental oxygen was 4.0 (2.0-6.0) days for the colchicine group and 6.5 (4.0-9.0) days for the placebo group ($p < 0.001$). Median (IQR) time of hospitalisation was 7.0 (5.0-9.0) days for the colchicine group and 9.0 (7.0-12.0) days for the placebo group ($p = 0.003$). At day 2, 67% versus 86% of patients maintained the need for supplemental oxygen, while at day 7, the values were 9% versus 42%, in the colchicine and the placebo groups, respectively (log rank; $p = 0.001$). Two patients died, both in placebo group. Diarrhoea was more frequent in the colchicine group ($p = 0.26$). Colchicine reduced the length of both, supplemental oxygen therapy and hospitalisation. The drug was safe and well tolerated. Once death was an uncommon event, it is not possible to ensure that colchicine reduced mortality of COVID-19.

40. **Non-invasive positive pressure ventilation versus endotracheal intubation in treatment of COVID-19 patients requiring ventilatory support.** Daniel P, Mecklenburg M, Massiah C, et al. *Am J Emerg Med*. 2021 Jan 29;43:103-108. doi: 10.1016/j.ajem.2021.01.068.

<https://www.sciencedirect.com/science/article/pii/S0735675721000711>

Findings: A total of 222 were enrolled. Overall mortality was 77.5%. Mortality for intubation-first group was 82%, for Intubation after NIV was 84%, and for NIV-only was 69%. In multivariable analysis, NIV-only was associated with decreased all-cause mortality. No difference in mortality was observed between intubation-first and intubation after NIV. Secondary analysis found all patients who received NIV to have lower mortality than patients who were intubated only. Utilization of NIV as the initial intervention in COVID-19 patients requiring ventilatory support is associated with significant survival benefit. For patients intubated after NIV, the mortality rate is not worse than those who undergo intubation as their initial intervention.

41. **Summary of adverse drug events for hydroxychloroquine, azithromycin, and chloroquine during the COVID-19 pandemic.** Dauner DG, Dauner KN. *J Am Pharm Assoc*. 2021 Jan 11:S1544-3191(21)00008-X. doi: 10.1016/j.japh.2021.01.007. [https://www.japha.org/article/S1544-3191\(21\)00008-X/fulltext](https://www.japha.org/article/S1544-3191(21)00008-X/fulltext)

Findings: There was a statistically significant increasing trend in the reported ADEs for both HCQ and AZM. Before the declaration of the national emergency, there were 592 reported drug-ADE pairs for the 3 drugs compared with 2492 drug-ADE pairs reported after March 13, 2020. These 2492 drug-ADE pairs represented 848 ADEs across the 3 drugs, of which 114 (13.4%) were identified as potential signals including 55 (48.2%) that were not listed in the prescribing information. Our results showed that the reported ADEs for HCQ and AZM have increased during the COVID-19 pandemic. Differences were observed in both the type of and frequency of

the highest reported ADEs for the 3 selected drugs before and after the national emergency declaration. Although causation cannot be determined from ADE reports, further investigation of some reports may be warranted. Our results highlight the need for pharmacovigilance and education of health care professionals on the safety of these drugs when being used for COVID-19 prophylaxis or treatment.

42. **Peginterferon lambda for the treatment of outpatients with COVID-19: a phase 2, placebo-controlled randomised trial.** Feld JJ et al. *Lancet Respir Med* 2021 Feb 5. doi:

[https://doi.org/10.1016/S2213-2600\(20\)30566-X](https://doi.org/10.1016/S2213-2600(20)30566-X)

[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30566-X/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30566-X/fulltext)

Findings. Between May 18, and Sept 4, 2020, we recruited 30 patients per group. The decline in SARS-CoV-2 RNA was greater in those treated with peginterferon lambda than placebo from day 3 onwards, with a difference of 2.42 log copies per mL at day 7. By day 7, 24 (80%) participants in the peginterferon lambda group had an undetectable viral load, compared with 19 (63%) in the placebo group ($p=0.15$). After controlling for baseline viral load, patients in the peginterferon lambda group were more likely to have undetectable virus by day 7 than were those in the placebo group. Of those with baseline viral load above 10⁶ copies per mL, 15 (79%) of 19 patients in the peginterferon lambda group had undetectable virus on day 7, compared with six (38%) of 16 in the placebo group. Peginterferon lambda was well tolerated, and adverse events were similar between groups with mild and transient aminotransferase, concentration increases more frequently observed in the peginterferon lambda group. Two individuals met the threshold of grade 3 increase, one in each group, and no other grade 3 or 4 laboratory adverse events were reported. Peginterferon lambda accelerated viral decline in outpatients with COVID-19, increasing the proportion of patients with viral clearance by day 7, particularly in those with high baseline viral load. Peginterferon lambda has potential to prevent clinical deterioration and shorten duration of viral shedding.

43. **Real-World Inpatient Use of Medications Repurposed for Coronavirus Disease 2019 in United States Hospitals, March-May 2020.** Kadri SS, Demirkale CY, Sun J, et al. *Open Forum Infect Dis.* 2020 Dec 15;8(2):ofaa616. doi: 10.1093/ofid/ofaa616. eCollection 2021 Feb.

<https://academic.oup.com/ofid/article/8/2/ofaa616/6034780>

Findings: We report off-label use patterns for medications repurposed for coronavirus disease 2019 (COVID-19) at 318 US hospitals. Inpatient hydroxychloroquine use declined by 80%, whereas corticosteroids and tocilizumab were initiated 2 days earlier in May versus March 2020. Two thirds of ventilated COVID-19 patients were already receiving corticosteroids during March-May 2020, resembling pre-COVID use in mechanically ventilated influenza patients.

44. **Comparison of Associations between Glucocorticoids Treatment and Mortality in COVID-19 Patients and SARS Patients: A Systematic Review and Meta-Analysis.** Li J, Liao X, Zhou Y, et al. *Shock.* 2021 Feb 3. doi: 10.1097/SHK.0000000000001738.

Findings: Ten trials and 71 observational studies, with a total of 45,935 patients, were identified. Glucocorticoids treatment, was associated with decreased all-cause mortality both in COVID-19 and SARS, based on high quality evidence, as well as decreased all-cause mortality-including composite outcome of COVID-19. In subgroup analyses, all-cause mortality was

significantly lower among COVID-19 patients being accompanied by severe ARDS but not mild ARDS, taking low-dose or pulse glucocorticoids, being critically severe but not only severe, being of critical severity and old but not young, being of critical severity and men but not women, non-early taking glucocorticoids, taking dexamethasone or methylprednisolone, and with the increased inflammatory state; but for SARS, lower mortality was observed among those who were taking medium-high dose glucocorticoids, being severe or critically severe, early taking glucocorticoids, and taking methylprednisolone or prednisolone. Glucocorticoids treatment reduced mortality in COVID-19 and SARS patients of critical severity; however, different curative effects existed between the two diseases among subpopulations, mainly regarding sex- and age-specific effects, optimal doses and use timing of glucocorticoids.

45. **Outcomes of Patients with Coronavirus Disease 2019 Receiving Organ Support Therapies: The International Viral Infection and Respiratory Illness Universal Study Registry.** Domecq JP, Lal A, Sheldrick CR, et al. *Crit Care Med.* 2021 Jan 28. doi: 10.1097/CCM.0000000000004879. https://journals.lww.com/ccmjournal/Abstract/9000/Outcomes_of_Patients_With_Coronavirus_Disease_2019.95368.aspx

Findings: Among 20,608 patients with coronavirus disease 2019, the mean age was 60.5, 11,1887 (54.3%) were men, 8,745 (42.4%) were admitted to the ICU, and 3,906 (19%) died in the hospital. Hospital mortality was 8.2% for patients receiving no organ support (n = 15,001). The most common organ support therapy was invasive mechanical ventilation (n = 5,005; 24.3%), with a hospital mortality of 49.8%. Mortality ranged from 40.8% among patients receiving only invasive mechanical ventilation (n = 1,749) to 71.6% for patients receiving invasive mechanical ventilation, vasoactive drugs, and new renal replacement therapy (n = 655). Mortality was 39% for patients receiving extracorporeal membrane oxygenation (n = 389). Rates of discharge home ranged from 73.5% for patients who did not require organ support therapies to 29.8% for patients who only received invasive mechanical ventilation, and 8.8% for invasive mechanical ventilation, vasoactive drugs, and renal replacement; 10.8% of patients older than 74 years who received invasive mechanical ventilation were discharged home. Median hospital length of stay for patients on mechanical ventilation was 17.1 days (9.7-28 d). Adjusted interhospital variation in mortality among patients receiving invasive mechanical ventilation was large (median odds ratio 1.69). Coronavirus disease 2019 prognosis varies by age and level of organ support. Interhospital variation in mortality of mechanically ventilated patients was not explained by patient characteristics and requires further evaluation.

Transmission / Infection Control

46. **Quantitative Assessment of Viral Dispersion Associated with Respiratory Support Devices in a Simulated Critical Care Environment.** Avari H, Hiebert RJ, Ryzynski AA, et al. *Am J Respir Crit Care Med.* 2021 Feb 3. doi: 10.1164/rccm.202008-3070OC. <https://www.atsjournals.org/doi/abs/10.1164/rccm.202008-3070OC>

Findings: Invasive ventilation and helmet ventilation with a PEEP valve were associated with the lowest bacteriophage concentrations in the air, and high-flow nasal oxygen and nasal prongs the highest. At the intubating position, bacteriophage concentrations associated with high-flow nasal oxygen (2.66×10^4 PFU/L of air sampled), nasal prongs (1.60×10^4 PFU/L of air sampled),

non-rebreather facemask (7.87×10^2 PFU/L of air sampled), and BiPAP (1.91×10^2 PFU/L of air sampled) were significantly higher when compared to invasive ventilation (each $P < 0.05$). The difference between bacteriophage concentrations associated with helmet ventilation with a PEEP valve (4.29×10^{-1} PFU/L of air sampled) and invasive ventilation was not statistically significant.

47. **Transmission of COVID-19 in 282 clusters in Catalonia, Spain: a cohort study.** Marks M, Millat-Martinez P, et al. *Lancet Infect Dis.* 2021 Feb 2:S1473-3099(20)30985-3. doi: 10.1016/S1473-3099(20)30985-3. [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30985-3/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30985-3/fulltext)

FINDINGS: We identified 314 patients with COVID-19, with 282 (90%) having at least one contact (753 contacts in total), resulting in 282 clusters. 90 (32%) of 282 clusters had at least one transmission event. The secondary attack rate was 17% (125 of 753 contacts), with a variation from 12% when the index case had a viral load lower than 1×10^6 copies per mL to 24% when the index case had a viral load of 1×10^{10} copies per mL or higher. Increased risk of transmission was also associated with household contact (3.0, 1.59-5.65) and age of the contact (per year: 1.02, 1.01-1.04). In our study, the viral load of index cases was a leading driver of SARS-CoV-2 transmission. The risk of symptomatic COVID-19 was strongly associated with the viral load of contacts at baseline and shortened the incubation time of COVID-19 in a dose-dependent manner.

Vaccines

48. **The E484K mutation in the SARS-CoV-2 spike protein reduces but does not abolish neutralizing activity of human convalescent and post-vaccination sera.** Jangra S, Ye C, Rathnasinghe R, et al. *medRxiv. PREPRINT.* 2021 Jan 29:2021.01.26.21250543. doi: 10.1101/2021.01.26.21250543.

<https://www.medrxiv.org/content/10.1101/2021.01.26.21250543v1.full.pdf>

Findings: One year in the coronavirus disease 2019 (COVID-19) pandemic, the first vaccines are being rolled out under emergency use authorizations. It is of great concern that newly emerging variants of SARS-CoV-2 can escape antibody-mediated protection induced by previous infection or vaccination through mutations in the spike protein. The glutamate (E) to Lysine (K) substitution at position 484 (E484K) in the receptor binding domain (RBD) of the spike protein is present in the rapidly spreading variants of concern belonging to the B.1.351 and P.1 lineages. We performed in vitro microneutralization assays with both the USA-WA1/2020 virus and a recombinant (r)SARS-CoV-2 virus that is identical to USA-WA1/2020 except for the E484K mutation introduced in the spike RBD. We selected 34 sera from study participants based on their SARS-CoV-2 spike ELISA antibody titer (negative [N=4] versus weak [N=8], moderate [N=11] or strong positive [N=11]). In addition, we included sera from five individuals who received two doses of the Pfizer SARS-CoV-2 vaccine BNT162b2. Serum neutralization efficiency was lower against the E484K rSARS-CoV-2 (vaccination samples: 3.4 fold; convalescent low IgG: 2.4 fold, moderate IgG: 4.2 fold and high IgG: 2.6 fold) compared to USA-WA1/2020. For some of the convalescent donor sera with low or moderate IgG against the SARS-CoV-2 spike, the drop in neutralization efficiency resulted in neutralization ID50 values similar to negative

control samples, with low or even absence of neutralization of the E484K rSARS-CoV-2. However, human sera with high neutralization titers against the USA-WA1/2020 strain were still able to neutralize the E484K rSARS-CoV-2. Therefore, it is important to aim for the highest titers possible induced by vaccination to enhance protection against newly emerging SARS-CoV-2 variants. Two vaccine doses may be needed for induction of high antibody titers against SARS-CoV-2. Postponing the second vaccination is suggested by some public health authorities in order to provide more individuals with a primer vaccination. *Our data suggests that this may leave vaccinees less protected against newly emerging variants.*

49. Neutralization of SARS-CoV-2 spike 69/70 deletion, E484K and N501Y variants by BNT162b2 vaccine-elicited sera. Xie, X., Liu, Y., Liu, J. et al. *Nat Med* (2021).

<https://doi.org/10.1038/s41591-021-01270-4>

Findings: We engineered three SARS-CoV-2 viruses containing key spike mutations from the newly emerged United Kingdom (UK) and South African (SA) variants: N501Y from UK and SA; 69/70-deletion + N501Y + D614G from UK; and E484K + N501Y + D614G from SA. Neutralization geometric mean titers (GMTs) of 20 BNT162b2 vaccine-elicited human sera against the three mutant viruses were 0.81- to 1.46-fold of the GMTs against parental virus, indicating small effects of these mutations on neutralization by sera elicited by two BNT162b2 doses.

50. Single Dose Administration, And the Influence of the Timing of the Booster Dose on Immunogenicity and Efficacy of ChAdOx1 nCoV-19 (AZD1222) Vaccine. Voysey M et al.

PREPRINT. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3777268

Findings: We present data from phase III efficacy trials of ChAdOx1 nCoV-19 in the United Kingdom and Brazil, and phase I/II clinical trials in the UK and South Africa, against symptomatic disease caused by SARS-CoV-2. ChAdOx1 nCoV-19 vaccination programmes aimed at vaccinating a large proportion of the population with a single dose, with a second dose given after a 3 month period is an effective strategy for reducing disease, and may be the optimal for rollout of a pandemic vaccine when supplies are limited in the short term.

51. Should Antipyretics be used to Relieve Acute Adverse Events Related to COVID-19 Vaccines?

Etminan M, Sodhi M, Ganjizadeh-Zavareh S. *Chest*. 2021 Feb 4:S0012-3692(21)00254-3. doi: 10.1016/j.chest.2021.01.080.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7862017/pdf/main.pdf>

Findings: To date, no study has specifically examined the effect antipyretics on the immunogenicity of the COVID-19 vaccines. A recent report from the ½ single-blind randomised trial of the AstraZeneca (adenovirus-vectored vaccine) does mention that prophylactic use of acetaminophen did not interfere with the vaccine's immunogenicity although no data were provided, and these results might not be applicable to other mRNA type vaccines. Furthermore, there was no data provided on the use of antipyretics in the Moderna trial, while the Pfizer trial only mentioned that the use of antipyretics was increased with increasing dose concentrations and dose number, but data on immunogenicity were not given.

52. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy adults aged 60 years and older: a randomised, double-blind, placebo-controlled,

phase 1/2 clinical trial. Wu Z, Hu Y, Xu M, et al. *Lancet Infect Dis*. 2021 Feb 3:S1473-3099(20)30987-7. doi: 10.1016/S1473-3099(20)30987-7.

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30987-7/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30987-7/fulltext)

Findings: We did a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial of CoronaVac in healthy adults aged 60 years and older in Renqiu (Hebei, China). Vaccine or placebo was given by intramuscular injection in two doses (days 0 and 28). Phase 1 comprised a dose-escalation study, in which participants were allocated to two blocks: block 1 (3 µg inactivated virus in 0.5 mL of aluminium hydroxide solution per injection) and block 2 (6 µg per injection). Within each block, participants were randomly assigned (2:1) using block randomisation to receive CoronaVac or placebo (aluminium hydroxide solution only). In phase 2, participants were randomly assigned (2:2:2:1) using block randomisation to receive either CoronaVac at 1.5 µg, 3 µg, or 6 µg per dose, or placebo. All participants, investigators, and laboratory staff were masked to treatment allocation. The primary safety endpoint was adverse reactions within 28 days after each injection in all participants who received at least one dose. The primary immunogenicity endpoint was seroconversion rate at 28 days after the second injection (which was assessed in all participants who had received the two doses of vaccine according to their random assignment, had antibody results available, and did not violate the trial protocol). Seroconversion was defined as a change from seronegative at baseline to seropositive for neutralising antibodies to live SARS-CoV-2 (positive cutoff titre 1/8), or a four-fold titre increase if the participant was seropositive at baseline. Between May 22 and June 1, 2020, 72 participants (24 in each intervention group and 24 in the placebo group; mean age 65.8 years [SD 4.8]) were enrolled in phase 1, and between June 12 and June 15, 2020, 350 participants were enrolled in phase 2 (100 in each intervention group and 50 in the placebo group; mean age 66.6 years [SD 4.7] in 349 participants). In the safety populations from both phases, any adverse reaction within 28 days after injection occurred in 20 (20%) of 100 participants in the 1.5 µg group, 25 (20%) of 125 in the 3 µg group, 27 (22%) of 123 in the 6 µg group, and 15 (21%) of 73 in the placebo group. All adverse reactions were mild or moderate in severity and injection site pain (39 [9%] of 421 participants) was the most frequently reported event. As of Aug 28, 2020, eight serious adverse events, considered unrelated to vaccination, have been reported by seven (2%) participants. In phase 1, seroconversion after the second dose was observed in 24 of 24 participants (100.0% [95% CI 85.8-100.0]) in the 3 µg group and 22 of 23 (95.7% [78.1-99.9]) in the 6 µg group. In phase 2, seroconversion was seen in 88 of 97 participants in the 1.5 µg group (90.7% [83.1-95.7]), 96 of 98 in the 3 µg group (98.0% [92.8-99.8]), and 97 of 98 (99.0% [94.5-100.0]) in the 6 µg group. There were no detectable antibody responses in the placebo groups. CoronaVac is safe and well tolerated in older adults.

53. **Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia.** Gam-COVID-Vac Vaccine Trial Group. *Lancet*. 2021 Feb 2:S0140-6736(21)00234-8. doi: 10.1016/S0140-6736(21)00234-8. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00234-8/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00234-8/fulltext)

BACKGROUND: A heterologous recombinant adenovirus (rAd)-based vaccine, Gam-COVID-Vac (Sputnik V), showed a good safety profile and induced strong humoral and cellular immune responses in participants in phase 1/2 clinical trials. Here, we report preliminary results on the

efficacy and safety of Gam-COVID-Vac from the interim analysis of this phase 3 trial. We did a randomised, double-blind, placebo-controlled, phase 3 trial at 25 hospitals and polyclinics in Moscow, Russia. We included participants aged at least 18 years, with negative SARS-CoV-2 PCR and IgG and IgM tests, no infectious diseases in the 14 days before enrolment, and no other vaccinations in the 30 days before enrolment. Participants were randomly assigned (3:1) to receive vaccine or placebo, with stratification by age group. Investigators, participants, and all study staff were masked to group assignment. The vaccine was administered (0.5 mL/dose) intramuscularly in a prime-boost regimen: a 21-day interval between the first dose (rAd26) and the second dose (rAd5), both vectors carrying the gene for the full-length SARS-CoV-2 glycoprotein S. The primary outcome was the proportion of participants with PCR-confirmed COVID-19 from day 21 after receiving the first dose. All analyses excluded participants with protocol violations: the primary outcome was assessed in participants who had received two doses of vaccine or placebo, serious adverse events were assessed in all participants who had received at least one dose at the time of database lock, and rare adverse events were assessed in all participants who had received two doses and for whom all available data were verified in the case report form at the time of database lock. FINDINGS: Between Sept 7 and Nov 24, 2020, 21 977 adults were randomly assigned to the vaccine group (n=16 501) or the placebo group (n=5476). 19 866 received two doses of vaccine or placebo and were included in the primary outcome analysis. From 21 days after the first dose of vaccine (the day of dose 2), 16 (0.1%) of 14 964 participants in the vaccine group and 62 (1.3%) of 4902 in the placebo group were confirmed to have COVID-19; vaccine efficacy was 91.6% (95% CI 85.6-95.2). Most reported adverse events were grade 1 (7485 [94.0%] of 7966 total events). 45 (0.3%) of 16 427 participants in the vaccine group and 23 (0.4%) of 5435 participants in the placebo group had serious adverse events; none were considered associated with vaccination, with confirmation from the independent data monitoring committee. Four deaths were reported during the study (three [$<0.1\%$] of 16 427 participants in the vaccine group and one [$<0.1\%$] of 5435 participants in the placebo group), none of which were considered related to the vaccine. INTERPRETATION: This interim analysis of the phase 3 trial of Gam-COVID-Vac showed 91.6% efficacy against COVID-19 and was well tolerated in a large cohort.

54. Efficacy of ChAdOx1 nCoV-19 (AZD1222) Vaccine against SARS-CoV-2 VOC 202012/01

(B.1.1.7). Emary KRW et al. 2021 Feb 4. *PREPRINT*.

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3779160

Findings: A new variant of SARS-CoV-2, B.1.1.7, emerged as the dominant cause of COVID-19 infection in the United Kingdom from November 2020 with a transmission advantage over the previous variants of the virus. Here we report efficacy of the adenoviral vector vaccine, ChAdOx1 nCoV-19, against this variant in comparison with non-B.1.1.7 lineages. Between 1st October 2020 and 14th January 2021, 499 participants developed Covid-19infection. 1524 NAAT positive nose/throat swabs were collected from these participants during the trial. Of these, 323 swabs from 256 participants were successfully sequenced. ChAdOx1 nCoV-19 recipients had a significantly lower viral load as represented by minimum PCR Ct value ($p<0.0001$) and were NAAT positive for a shorter time ($p<0.0001$) than participants who received the control vaccine. Virus neutralisation activity by vaccine-induced antibodies was 9-fold lower against the B.1.1.7 variant than against a canonical non B.1.1.7 lineage. Vaccine

efficacy against symptomatic NAAT positive infection was similar for B.1.1.7 and non-B1.1.7 lineages (74.6% [95%CI 41.6-88.9] and 84% [95% CI 70.7-91.4] respectively). There was no difference in anti-spike antibody titres between individuals who had received a prior ChAdOx1 vectored vaccine and those who were naïve to ChAdOx1. Efficacy of ChAdOx1 nCoV-19 against the B.1.1.7 variant of SARS-CoV-2 is similar to the efficacy of the vaccine against other lineages. Furthermore, vaccination with ChAdOx1 nCoV-19 results in a reduction in the duration of shedding and viral load, which may translate into a material impact on transmission of disease.

55. **Management of Unilateral Axillary Lymphadenopathy Detected on Breast MRI in the Era of Coronavirus Disease (COVID-19) Vaccination.** Edmonds CE, Zuckerman SP, Conant EF. *AJR Am J Roentgenol.* 2021 Feb 5. doi: 10.2214/AJR.21.25604.

<https://www.ajronline.org/doi/pdf/10.2214/AJR.21.25604>

Findings: This article examines the available data on vaccine-related lymphadenopathy and offers a basic strategy to assess axillary lymphadenopathy on MRI and to guide management. At our institution, we are adding questions regarding the date(s) and laterality of administration of COVID-19 vaccination to our intake form before all breast imaging examinations. We consider MRI-detected isolated unilateral axillary lymphadenopathy ipsilateral to the vaccination arm to be most likely COVID-19 vaccine-related if within four weeks of either dose. In these cases, we assess the lymphadenopathy as BI-RADS 3 and recommend a follow-up ultrasound be performed within 6-8 weeks after the second dose. These guidelines may be refined as we gain further data on the expected time-course of axillary lymphadenopathy post COVID-19 vaccination. Until that time, this management pathway will help avoid unnecessary biopsies of benign vaccine-related reactive lymphadenopathy.

Whole Person Care

56. **The challenges of caring for people dying from COVID-19: a multinational, observational study (CovPall).** CovPall study team. *J Pain Symptom Manage.* 2021 Feb 5:S0885-3924(21)00159-7. doi: 10.1016/j.jpainsymman.2021.01.138.

<https://www.sciencedirect.com/science/article/pii/S0885392421001597?via%3Dihub>

Findings: We surveyed palliative care and hospice services, contacted via relevant organisations. 458 services responded; 277 UK, 85 rest of Europe, 95 rest of the world; 81% cared for patients with suspected or confirmed COVID-19, 77% had staff with suspected or confirmed COVID-19; 48% reported shortages of PPE, 40% staff shortages, 24% medicines shortages, 14% shortages of other equipment. Services provided direct care and education in symptom management and communication; 91% changed how they worked. Care often shifted to increased community and hospital care, with fewer admissions to inpatient palliative care units. Factors associated with increased odds of PPE shortages were: charity rather than public management, inpatient palliative care unit rather than other settings. Being outside the UK was associated with lower odds of staff shortages. Staff described increased workload, concerns for their colleagues who were ill, whilst expending time struggling to get essential equipment and medicines, perceiving they were not a front-line service. Palliative care services were often overwhelmed yet felt ignored in the COVID-19 response. Palliative care needs better

integration with health care systems when planning and responding to future epidemics/pandemics.

Women & Children

57. **SARS-CoV-2 transmission among children and staff in daycare centres during a nationwide lockdown in France: a cross-sectional, multicentre, seroprevalence study.** Lachassinne E et al. *Lancet Child & Adolescent Health* 2021 Feb 8. doi: [https://doi.org/10.1016/S2352-4642\(21\)00024-9](https://doi.org/10.1016/S2352-4642(21)00024-9)

Findings. Between June 4 and July 3, 2020, we enrolled 327 children (mean age 1·9 [SD 0·9] years; range 5 months to 4·4 years), 197 daycare centre staff (mean age 40 [12] years), and 164 adults in the comparator group (42 [12] years). Positive serological tests were observed for 14 children (raw seroprevalence 4·3%; 95% CI 2·6–7·1) and 14 daycare centre staff (7·7%; 4·2–11·6). After accounting for imperfect sensitivity and specificity of the assay, we estimated that 3·7% (95% credible interval [95% CrI] 1·3–6·8) of the children and 6·8% (3·2–11·5) of daycare centre staff had SARS-CoV-2 infection. The comparator group fared similarly to the daycare centre staff; nine participants had a positive serological test (raw seroprevalence 5·5%; 95% CI 2·9–10·1), leading to a seroprevalence of 5·0% (95% CrI 1·6–9·8) after accounting for assay characteristics. An exploratory analysis suggested that seropositive children were more likely than seronegative children to have been exposed to an adult household member with laboratory-confirmed COVID-19 (six [43%] of 14 vs 19 [6%] of 307). According to serological test results, the proportion of young children in our sample with SARS-CoV-2 infection was low. Intrafamily transmission seemed more plausible than transmission within daycare centres. Further epidemiological studies are needed to confirm this exploratory hypothesis.

GUIDELINES & CONSENSUS STATEMENTS

[Surviving Sepsis Campaign Guidelines on the Management of Adults with Coronavirus Disease 2019 \(COVID-19\) in the ICU: First Update.](#) Alhazzani W, Evans L, Alshamsi F, et al. *Crit Care Med.* 2021 Jan 28. doi: 10.1097/CCM.0000000000004899.

[Best-Practices for Preventing Skin Injury Beneath Personal Protective Equipment During the COVID-19 Pandemic: A Position Paper from the National Pressure Injury Advisory Panel \(NPIAP\).](#) National Pressure Injury Advisory Panel (NPIAP). *J Clin Nurs.* 2021 Feb 3. doi: 10.1111/jocn.15682.

[The COVID-19 vaccine in pregnancy: risks benefits and recommendations.](#) Stafford IA, Parchem JG, Sibai BM. *Am J Obstet Gynecol.* 2021 Jan 30:S0002-9378(21)00077-6. doi: 10.1016/j.ajog.2021.01.022.

[Update Alert 7: Epidemiology of and Risk Factors for Coronavirus Infection in Health Care Workers.](#) Chou R, Dana T, Buckley DI, et al. *Ann Intern Med.* 2021 Feb 9. doi: 10.7326/L21-0034.

CDC - [US COVID-19 Cases Caused by Variants](#)

FDA - [Using Ventilator Splitters During the COVID-19 Pandemic - Letter to Health Care Providers](#)

FDA - [Letter of Authorization, Reissuance of Convalescent Plasma EUA February 4, 2021](#)

FDA - [Coronavirus \(COVID-19\) Update: FDA Announces Advisory Committee Meeting to Discuss Janssen Biotech Inc.'s COVID-19 Vaccine Candidate](#)

NIH - [The COVID-19 Treatment Guidelines Panel's Statement on the Use of Tocilizumab \(and Other Interleukin-6 Inhibitors\) for the Treatment of COVID-19](#)

Commentary & News

[South Africa suspends use of AstraZeneca's COVID-19 vaccine after it fails to clearly stop virus varian](#)

[FACT SHEET: President Biden Announces Increased Vaccine Supply, Initial Launch of the Federal Retail Pharmacy Program, and Expansion of FEMA Reimbursement to States](#)

[COVID-19 Vaccine AstraZeneca confirms 100% protection against severe disease, hospitalisation and death in the primary analysis of Phase III trials](#)

[The Virus Variant Spreading in Britain May Make Vaccines Less Effective, Study Shows](#)

[Covid-19: Risk of aerosol transmission to staff outside of intensive care is likely to be higher than predicted.](#) Torjesen I. *BMJ*. 2021 Feb 5;372:n354. doi: 10.1136/bmj.n354.

[Johnson & Johnson Announces Submission of Application to the U.S. FDA for Emergency Use Authorization of its Investigational Single-Shot Janssen COVID-19 Vaccine Candidate](#)

New York Times: [A Few Covid Vaccine Recipients Developed a Rare Blood Disorder; A link to the vaccines is not certain, and investigations are underway in some reported cases](#)

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