

COVID-19 Resource Desk

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New Research

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Basic Science / Virology / Pre-clinical

- 1. Baricitinib treatment resolves lower-airway macrophage inflammation and neutrophil recruitment in SARS-CoV-2-infected rhesus macaques.** Hoang TN, Pino M, Boddapati AK, et al. *Cell*. 2020 Nov 10:S0092-8674(20)31466-5. doi: 10.1016/j.cell.2020.11.007. [https://www.cell.com/cell/fulltext/S0092-8674\(20\)31466-5](https://www.cell.com/cell/fulltext/S0092-8674(20)31466-5)
Findings: SARS-CoV-2-induced hypercytokinemia and inflammation are critically associated with COVID-19 severity. Baricitinib, a clinically approved JAK1/JAK2 inhibitor, is currently being investigated in COVID-19 clinical trials. Here, we investigated the immunologic and virologic efficacy of baricitinib in a rhesus macaque model of SARS-CoV-2 infection. Viral shedding measured from nasal and throat swabs, bronchoalveolar lavages, and tissues was not reduced with baricitinib. Type I interferon (IFN) antiviral responses and SARS-CoV-2-specific T cell responses remained similar between the two groups. Animals treated with baricitinib showed reduced inflammation, decreased lung infiltration of inflammatory cells, reduced NETosis activity, and more limited lung pathology. Importantly, baricitinib-treated animals had a rapid and remarkably potent suppression of lung macrophage production of cytokines and chemokines responsible for inflammation and neutrophil recruitment. These data support a beneficial role for, and elucidate the immunological mechanisms underlying, the use of baricitinib as a frontline treatment for inflammation induced by SARS-CoV-2 infection.

Clinical Syndrome

- 2. Can COVID-19 be a risk for cachexia for patients during intensive care? Narrative review and nutritional recommendations.** Virgens IPA, Santana NM, Lima SCVC, Fayh APT. *Br J Nutr*. 2020 Nov 5:1-9. doi: 10.1017/S0007114520004420. <https://www.cambridge.org/core/journals/british-journal-of-nutrition/article/can-covid19-be-a-risk-for-cachexia-for-patients-during-intensive-care-narrative-review-and-nutritional-recommendations/83E3C47138C8A30A64B2543B20238B69>
Findings: The aim of this article was to establish possible connections between COVID-19, prolonged hospitalisation and muscle wasting, as well as to propose nutritional recommendations for the prevention and treatment of cachexia, through a narrative review.

Identification of risk and presence of malnutrition should be an early step in general assessment of all patients, with regard to more at-risk categories including older adults and individuals suffering from chronic and acute disease conditions, such as COVID-19. The deterioration of nutritional status, and consequently cachexia, increases the risk of mortality and needs to be treated with attention as other complications. There is, however, little hard evidence of nutritional approaches in assisting COVID-19 treatment or its management including cachexia.

3. **Characteristics of Adults aged 18-49 Years without Underlying Conditions Hospitalized with Laboratory-Confirmed COVID-19 in the United States, COVID-NET - March-August 2020.** COVID-NET Surveillance Team. *Clin Infect Dis*. 2020 Dec 3;ciaa1806. doi: 10.1093/cid/ciaa1806. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1806/6017811>
Findings: Among 513 adults aged 18-49 years without underlying medical conditions hospitalized with COVID-19 during March-August 2020, 22% were admitted to intensive care unit; 10% required mechanical ventilation; and three patients died (0.6%). These data demonstrate that healthy younger adults can develop severe COVID-19.
4. **Acute Cerebrovascular Disorders and Vasculopathies Associated with Significant Mortality in SARS-CoV-2 Patients Admitted to The Intensive Care Unit in The New York Epicenter.** Al-Mufti F, Becker C, Kamal H, et al. *J Stroke Cerebrovasc Dis*. 2020 Nov 2;30(2):105429. doi: 10.1016/j.jstrokecerebrovasdis.2020.105429. <https://www.sciencedirect.com/science/article/pii/S1052305720308478>
Findings: We present a case series of consecutive COVID-19 patients with cerebrovascular disease treated at our institution including 3 cases of cerebral artery dissection including subarachnoid hemorrhage. Knowledge of the varied presentations including dissections will help treating clinicians at the bedside monitor and manage these complications preemptively.

Diagnosics & Screening

5. **Chest CT in COVID-19 at the ED: Validation of the COVID-19 Reporting and Data System (CO-RADS) and CT severity score.** Lieveld AWE, Azijli K, Teunissen BP, et al. *Chest*. 2020 Nov 30:S0012-3692(20)35311-3. doi: 10.1016/j.chest.2020.11.026. [https://journal.chestnet.org/article/S0012-3692\(20\)35311-3/fulltext](https://journal.chestnet.org/article/S0012-3692(20)35311-3/fulltext)
Findings: We aimed to prospectively validate the CO-RADS as a COVID-19 diagnostic tool at the emergency department (ED), and evaluate if the CTSS is associated with prognosis. We conducted a prospective, observational study in two tertiary centers in The Netherlands, between March 19 and May 28, 2020. We consecutively included 741 adult patients at the ED with suspected COVID-19, who received a chest CT and SARS-CoV-2 PCR. Diagnostic accuracy measures were calculated for CO-RADS using PCR as reference. 741 patients were included. We found an AUC of 0.91 for CO-RADS using PCR as reference. The optimal CO-RADS cut-off was 4, with a sensitivity of 89.4% and specificity of 87.2%. We found a significant association between CTSS and hospital admission, ICU admission, and 30-day mortality. Our findings support the use of CO-RADS and CTSS in triage, diagnosis and management decisions for patients presenting with possible COVID-19 at the ED.

6. **Viral cultures for COVID-19 infectious potential assessment - a systematic review.** Jefferson T, Spencer EA, Brassey J, Heneghan C. *Clin Infect Dis*. 2020 Dec 3:ciaa1764. doi: 10.1093/cid/ciaa1764. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1764/6018217>

Findings: We included 29 studies reporting attempts at culturing, or observing tissue infection by, SARS-CoV-2 in sputum, nasopharyngeal or oropharyngeal, urine, stool, blood and environmental specimens. The data suggest a relationship between the time from onset of symptom to the timing of the specimen test, cycle threshold (Ct) and symptom severity. Complete live viruses are necessary for transmission, not the fragments identified by PCR. Prospective routine testing of reference and culture specimens and their relationship to symptoms, signs and patient co-factors should be used to define the reliability of PCR for assessing infectious potential. Those with high cycle threshold are unlikely to have infectious potential.

Epidemiology & Public Health

7. **Increased Intensity of PCR Testing Reduced COVID-19 Transmission Within Countries During the First Pandemic Wave.** Rannan-Eliya RP, Wijemunige N, Gunawardana J, et al. *Health Aff (Millwood)*. 2020 Dec 2:101377hlthaff202001409. doi:10.1377/hlthaff.2020.01409. <https://www.healthaffairs.org/doi/10.1377/hlthaff.2020.01409>

Findings: Experts agree that PCR testing is critical in controlling COVID-19, but decision-makers disagree on how much testing is optimal. Controlling for interventions and ecological factors, we used linear regression to quantify testing's impact on COVID-19's average reproduction number, representing transmissibility, in 173 countries and territories, accounting for 99% of the world's COVID-19 cases, during March to June 2020. Amongst interventions, PCR testing had the greatest influence—a ten-fold increase in the ratio of tests to new cases reported reduced the average reproduction number by 9% across a range of testing levels. Our results imply that mobility reductions (e.g., shelter-in-place orders) were less effective in developing countries than in developed countries. Our results help explain how some nations achieved near-elimination of COVID-19 and the failure of lockdowns to slow COVID-19 in others. Our findings suggest that World Health Organization and other testing benchmarks are insufficient for COVID-19 control. Increased testing and isolation may represent the most effective, least costly alternative in terms of money, economic growth and human life for controlling COVID-19.

8. **Overdose-Related Cardiac Arrests Observed by Emergency Medical Services During the US COVID-19 Epidemic.** Friedman J, Beletsky L, Schriger DL. *JAMA Psychiatry*. Published online December 03, 2020. doi:10.1001/jamapsychiatry.2020.4218 <https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2773768>

Findings: We describe a large-magnitude, national surge in overdose-related cardiac arrest during the initial months of the COVID-19 epidemic in the US. Peak rates in May 2020 were more than double the baseline from 2018 and 2019, and overall 2020 values were elevated by approximately 50%. The temporal similarities to decreased mobility suggest that the fallout from the COVID-19 pandemic—perhaps especially social isolation—is sharply accelerating fatal

overdose trends. The lack of a commensurate sharp increase in total (fatal and nonfatal) overdose incidents could indicate a rising overdose case fatality rate in a context of more stable, albeit elevated, overdose rates. Many of the trends predicted by public health experts at the outset of the pandemic, such as an increased proportion of individuals using substances alone, increased toxification of the drug supply, and reduced access to treatment, could increase the lethality of each overdose incident.

9. **Impact of non-pharmaceutical interventions targeted at COVID-19 pandemic on influenza burden - a systematic review.** Fricke LM, Glöckner S, Dreier M, Lange B. *J Infect.* 2020 Dec 2:S0163-4453(20)30756-8. doi: 10.1016/j.jinf.2020.11.039.

[https://www.journalofinfection.com/article/S0163-4453\(20\)30756-8/fulltext](https://www.journalofinfection.com/article/S0163-4453(20)30756-8/fulltext)

Findings: We included 23 records reporting from 15 countries/regions as well as 8 reports from European Public Health agencies. Estimates in the 2019/2020 season based on influenza virus tests (4 out of 7 countries/regions), defined influenza cases (8 out of 9), influenza positivity rate (7 out of 8), and severe complications (1 out of 2) were lower than in former seasons. Results from syndromic indicators, such as influenza-like-illness (ILI), were less clear or even raised (4 out of 7) after the influenza season indicating a misclassification with COVID-19 cases. Evidence synthesis suggests that NPIs targeted at SARS-CoV-2-transmission reduce influenza burden as well. Low threshold NPIs need to be more strongly emphasized in influenza prevention strategies.

Healthcare Delivery & Healthcare Workers

10. **Infection and mortality of healthcare workers worldwide from COVID-19: a systematic review.** Bandyopadhyay S, Baticulon RE, Kadhum M, et al. *BMJ Glob Health.* 2020 Dec;5(12):e003097. doi: 10.1136/bmjgh-2020-003097.

<https://gh.bmj.com/content/5/12/e003097>

Findings: A total of 152 888 infections and 1413 deaths were reported. Infections were mainly in women (71.6%, n=14 058) and nurses (38.6%, n=10 706), but deaths were mainly in men (70.8%, n=550) and doctors (51.4%, n=525). Limited data suggested that general practitioners and mental health nurses were the highest risk specialities for deaths. There were 37.2 deaths reported per 100 infections for HCWs aged over 70 years. Europe had the highest absolute numbers of reported infections (119 628) and deaths (712), but the Eastern Mediterranean region had the highest number of reported deaths per 100 infections (5.7). COVID-19 infections and deaths among HCWs follow that of the general population around the world. The reasons for gender and specialty differences require further exploration, as do the low rates reported in Africa and India. Although physicians working in certain specialities may be considered high risk due to exposure to oronasal secretions, the risk to other specialities must not be underestimated. Elderly HCWs may require assigning to less risky settings such as telemedicine or administrative positions. Our pragmatic approach provides general trends and highlights the need for universal guidelines for testing and reporting of infections in HCWs.

Laboratory Results

- 11. Frequency of Positive Aspergillus Tests in COVID-19 Patients in Comparison to Other Patients with Pulmonary Infections Admitted to the ICU.** Yusuf E, Vonk A, van den Akker JPC, et al. *J Clin Microbiol.* 2020 Dec 4;JCM.02278-20. doi: 10.1128/JCM.02278-20.
<https://jcm.asm.org/content/jcm/early/2020/12/04/JCM.02278-20.full.pdf>

Findings: We compared the proportion of positive Aspergillus tests in COVID-19 patients admitted to the ICU for > 24 hours with two control groups; patients with community acquired pneumonia with 1. a PCR confirmed influenza infection (considered as 'positive' control since the link between influenza and invasive aspergillosis has been established), and 2. Streptococcus pneumoniae pneumonia (in whom positive Aspergillus tests are mostly considered as colonisation). During the study period, 92 COVID-19 patients, 48 influenza and 65 pneumococcal pneumonia patients were identified. Any positive Aspergillus test from any respiratory sample was found in 10.9% of the COVID-19 patients, 6.2% of the patients with pneumococcal pneumonia and 22.9% of those infected with influenza. A positive culture or PCR or galactomannan test on bronchoalveolar lavage fluid (BAL) only was found in 5.4% of COVID-19 patients, which was lower than in patients with influenza (18.8%) and comparable to pneumococcal pneumonia group (4.6%). In conclusion, in COVID19 patients, the prevalence of a positive aspergillus test was comparable to patients with admitted for pneumococcal pneumonia but substantially lower than what we observed in patients with influenza.
- 12. Dynamics and Correlation among Viral Positivity, Seroconversion, and Disease Severity in COVID-19: A Retrospective Study.** Fu Y, Li Y, Guo E, et al. *Ann Intern Med.* 2020 Dec 8. doi: 10.7326/M20-3337. <https://www.acpjournals.org/doi/10.7326/M20-3337>

Findings: Among 12 780 reverse transcriptase PCR tests for severe acute respiratory syndrome coronavirus 2 that were done, 24.0% had positive results. In 2142 patients with laboratory-confirmed COVID-19, the viral positivity rate peaked within the first 3 days. The median duration of viral positivity was 24.0 days in critically ill patients and 18.0 days in noncritically ill patients. Being critically ill was an independent risk factor for longer viral positivity. In patients with laboratory-confirmed COVID-19, the IgM-positive rate was 19.3% in the first week, peaked in the fifth week (81.5%), and then decreased steadily to around 55% within 9 to 10 weeks. The IgG-positive rate was 44.6% in the first week, reached 93.3% in the fourth week, and then remained high. Similar antibody responses were seen in clinically diagnosed cases. Serum inflammatory markers remained higher in critically ill patients. Among noncritically ill patients, a higher proportion of those with persistent viral positivity had low IgM titers (<100 AU/mL) during the entire course compared with those with short viral positivity. The rate of viral PCR positivity peaked within the initial few days. Seroconversion rates peaked within 4 to 5 weeks. Dynamic laboratory index changes corresponded well to clinical signs, the recovery process, and disease severity. Low IgM titers (<100 AU/mL) are an independent risk factor for persistent viral positivity.

Prognosis

13. **Clinical characteristics on admission predict in-hospital fatal outcome in patients aged ≥ 75 years with novel coronavirus disease (COVID-19): a retrospective cohort study.** Yu Z, Ke Y, Xie J, et al. *BMC Geriatr.* 2020 Nov 30;20(1):514. doi: 10.1186/s12877-020-01921-0.
<https://bmgeriatr.biomedcentral.com/articles/10.1186/s12877-020-01921-0>
Findings: In-hospital fatality among elderly COVID-19 patients can be estimated by sex and on-admission measurements of body temperature, SpO₂, and NT-proBNP.

14. **Association between statin use and outcomes in patients with coronavirus disease 2019 (COVID-19): a nationwide cohort study.** Butt JH, Gerds TA, Schou M, et al. *BMJ Open.* 2020 Dec 4;10(12):e044421. doi: 10.1136/bmjopen-2020-044421.
<https://bmjopen.bmj.com/content/10/12/e044421>
Findings: The study population comprised 4842 patients with COVID-19 (median age 54 years, 47.1% men), of whom 843 (17.4%) redeemed a prescription of statins. Patients with statin exposure were more often men and had a greater prevalence of comorbidities. The median follow-up was 44 days. After adjustment for age, sex, ethnicity, socioeconomic status and comorbidities, statin exposure was not associated with a significantly different risk of mortality. The results were consistent across subgroups of age, sex and presumed indication for statin therapy. Among patients with statin exposure, there was no difference between statin drug or treatment intensity with respect to outcomes. Recent statin exposure in patients with COVID-19 infection was not associated with an increased or decreased risk of all-cause mortality or severe infection.

15. **Dementia and outcomes from coronavirus disease 2019 (COVID-19) pneumonia: A systematic review and meta-analysis.** Hariyanto TI, Putri C, Arisa J, et al. *Arch Gerontol Geriatr.* 2020 Nov 19;93:104299. doi: 10.1016/j.archger.2020.104299.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7674980/>
Findings: A total of 24 studies with 46,391 dementia patients were included in this meta-analysis and showed that dementia was associated with composite poor outcome. Extra care and close monitoring should then be provided to patients with dementia to minimize the risk of infections, preventing the development of severe and mortality outcomes.

Survivorship & Rehabilitation

16. **Persistent symptoms 1.5-6 months after COVID-19 in non-hospitalised subjects: a population-based cohort study.** Stavem K, Ghanima W, Olsen MK, et al. *Thorax.* 2020 Dec 3:thoraxjnl-2020-216377. doi: 10.1136/thoraxjnl-2020-216377.
<https://thorax.bmj.com/content/thoraxjnl/early/2020/12/02/thoraxjnl-2020-216377.full.pdf>
Findings: We invited 938 subjects; 451 (48%) responded. They reported less symptoms after 1.5-6 months than during COVID-19. 53% of women and 67% of men were symptom free, while 16% reported dyspnoea, 12% loss/disturbance of smell, and 10% loss/disturbance of taste. In multivariable analysis, having persistent symptoms was associated with the number of comorbidities and number of symptoms during the acute COVID-19 phase.

17. **A prospective study of 12-week respiratory outcomes in COVID-19-related hospitalisations.** Shah AS, Wong AW, Hague CJ, et al. *Thorax*. 2020 Dec 3:thoraxjnl-2020-216308. doi: 10.1136/thoraxjnl-2020-216308. <https://thorax.bmj.com/content/early/2020/12/02/thoraxjnl-2020-216308>
Findings: We describe the clinical, radiological and pulmonary function abnormalities that persist in previously hospitalised patients assessed 12 weeks after COVID-19 symptom onset and identify clinical predictors of respiratory outcomes. At least one pulmonary function variable was abnormal in 58% of patients and 88% had abnormal imaging on chest CT. There was strong association between days on oxygen supplementation during the acute phase of COVID-19 and both DLCO-% (diffusion capacity of the lung for carbon monoxide) predicted and total CT score. These findings highlight the need to develop treatment strategies and the importance of long-term respiratory follow-up after hospitalisation for COVID-19.
18. **Respiratory function in patients post-infection by COVID-19: a systematic review and meta-analysis.** Torres-Castro R, Vasconcello-Castillo L, Alsina-Restoy X, et al. *Pulmonology*. 2020 Nov 25:S2531-0437(20)30245-2. doi: 10.1016/j.pulmoe.2020.10.013. <https://www.sciencedirect.com/science/article/pii/S2531043720302452>
Findings: Post-infection COVID-19 patients showed impaired lung function; the most important of the pulmonary function tests affected was the diffusion capacity.
19. **Clinical status and lung function 10 weeks after severe SARS-CoV-2 infection.** Smet J, Stylemans D, Hanon S, et al. *Respir Med*. 2020 Nov 30;176:106276. doi: 10.1016/j.rmed.2020.106276. [https://www.resmedjournal.com/article/S0954-6111\(20\)30416-9/fulltext](https://www.resmedjournal.com/article/S0954-6111(20)30416-9/fulltext)
Findings: Two hundred-twenty subjects were evaluated at a median follow-up of 74±12 days. Forty-six percent of patients had normal lung function, while TLC and TLCO below the lower limit of normal were observed in 38% and 22% of subjects respectively. This restrictive pulmonary impairment was associated with length of hospital stay, admission to the intensive care unit, and invasive mechanical ventilation, but not with symptom score or CT score at baseline and follow-up. Fifty-four percent of COVID-19 survivors had abnormal lung function 10 weeks after diagnosis. Restriction was the most prevalent pulmonary function, with the more critically ill patients being more prone to this condition. Yet, restriction could not be linked with abnormal imaging results or residual symptoms.

Therapeutics

20. **Repurposed Antiviral Drugs for Covid-19 - Interim WHO Solidarity Trial Results.** WHO Solidarity Trial Consortium. *N Engl J Med*. 2020 Dec 2. doi: 10.1056/NEJMoa2023184. <https://www.nejm.org/doi/full/10.1056/NEJMoa2023184>
Findings: At 405 hospitals in 30 countries, 11,330 adults underwent randomization; 2750 were assigned to receive remdesivir, 954 to hydroxychloroquine, 1411 to lopinavir (without interferon), 2063 to interferon (including 651 to interferon plus lopinavir), and 4088 to no trial drug. Adherence was 94 to 96% midway through treatment, with 2 to 6% crossover. In total,

1253 deaths were reported (median day of death, day 8; interquartile range, 4 to 14). The Kaplan-Meier 28-day mortality was 11.8% (39.0% if the patient was already receiving ventilation at randomization and 9.5% otherwise). Death occurred in 301 of 2743 patients receiving remdesivir and in 303 of 2708 receiving its control, in 104 of 947 patients receiving hydroxychloroquine and in 84 of 906 receiving its control, in 148 of 1399 patients receiving lopinavir and in 146 of 1372 receiving its control, and in 243 of 2050 patients receiving interferon and in 216 of 2050 receiving its control. No drug definitely reduced mortality, overall or in any subgroup, or reduced initiation of ventilation or hospitalization duration. *These remdesivir, hydroxychloroquine, lopinavir, and interferon regimens had little or no effect on hospitalized patients with Covid-19, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay.*

21. **Combination of Tocilizumab and Steroids to Improve Mortality in Patients with Severe COVID-19 Infection: A Spanish, Multicenter, Cohort Study.** TOCICOV-study group. *Infect Dis Ther.* 2020 Dec 6. doi: 10.1007/s40121-020-00373-8.

<https://link.springer.com/article/10.1007/s40121-020-00373-8>

Findings: 506 patients with severe COVID-19 fulfilled the inclusion criteria. Among them, 268 were treated with tocilizumab and 238 patients were not. Median time to tocilizumab treatment from onset of symptoms was 11 days. Global mortality was 23.7%. Mortality was lower in patients treated with tocilizumab than in controls: 16.8% versus 31.5%). Tocilizumab treatment reduced mortality by 14.7% relative to no tocilizumab treatment. We calculated a number necessary to treat of 7. Among patients treated with steroids, mortality was lower in those treated with tocilizumab than in those treated with steroids alone. These results show that survival of patients with severe COVID-19 is higher in those treated with tocilizumab than in those not treated and that tocilizumab's effect adds to that of steroids administered to non-intubated patients with COVID-19 during the first 48 h of presenting with respiratory failure despite oxygen therapy. Randomised controlled studies are needed to confirm these results.

22. **Nutritional therapy for patients with coronavirus disease 2019 (COVID-19): Practical protocol from a single center highly affected by an outbreak of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.** Formisano E, Di Maio P, Ivaldi C, et al. *Nutrition.* 2020 Nov 6:111048. doi: 10.1016/j.nut.2020.111048.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7645291/>

Findings: The nutritional treatment was well tolerated by the patients. Of the non-ICU patients, 19.1% died. They were mainly women, with higher body mass indices and older in age. Of the patients in the ICU, 53.1% died. Of the 94 non-ICU patients, 72 scored positive on at least one nutritional risk screening item (excluding age). Of the 94 non-ICU patients, 68 were >70 y of age. Non-ICU patients whose energy and protein needs were not met were older and had a higher death rate than patients whose needs were met. This protocol should not be considered as a guideline; rather, it is intended to report the clinical experience of a nutrition team in an Italian reference center for the treatment of patients with COVID-19. Nutritional strategies should be implemented to prevent worsening of clinical outcomes.

23. **Mortality in tocilizumab-treated patients with COVID-19: a systematic review and meta-analysis.** Berardicurti O, Ruscitti P, Ursini F, et al. *Clin Exp Rheumatol*. 2020 Nov-Dec;38(6):1247-1254. Epub 2020 Dec 3. <https://www.clinexprheumatol.org/abstract.asp?a=16290>
Findings: We included 22 studies and 1520 TCZ-treated patients (mean age: 61 years). The mortality estimated pooled prevalence was 19% and improvement estimated pooled prevalence was 71%. Factors associated with the mortality are the number of patients in intensive care unit, the number of patients requiring invasive ventilation and the sera C-reactive protein value before TCZ administration. We observed a reduction in the odds of mortality in TCZ-treated patients when compared to those treated with other therapies. This study showed that the mortality pooled prevalence in TCZ-treated patients is lower than the overall mortality reported in patients with severe COVID-19.
24. **Hydroxychloroquine as Postexposure Prophylaxis to Prevent Severe Acute Respiratory Syndrome Coronavirus 2 Infection: A Randomized Trial.** Barnabas RV, Brown ER, Bershteyn A, et al. *Ann Intern Med*. 2020 Dec 8. doi: 10.7326/M20-6519. <https://www.acpjournals.org/doi/full/10.7326/M20-6519>
Findings: Between March and August 2020, 671 households were randomly assigned: 337 (407 participants) to the hydroxychloroquine group and 334 (422 participants) to the control group. Retention at day 14 was 91%, and 10 724 of 11 606 (92%) expected swabs were tested. Among the 689 (89%) participants who were SARS-CoV-2 negative at baseline, there was no difference between the hydroxychloroquine and control groups in SARS-CoV-2 acquisition by day 14 (53 versus 45 events). The frequency of participants experiencing adverse events was higher in the hydroxychloroquine group than the control group (66 [16.2%] versus 46 [10.9%], respectively). This rigorous randomized controlled trial among persons with recent exposure excluded a clinically meaningful effect of hydroxychloroquine as postexposure prophylaxis to prevent SARS-CoV-2 infection.
25. **COVID-19 Symptoms: Longitudinal Evolution and Persistence in Outpatient Settings.** Nehme M, Braillard O, Alcoba G, et al. *Ann Intern Med*. 2020 Dec 8. doi: 10.7326/M20-5926. <https://www.acpjournals.org/doi/10.7326/M20-5926>
Findings: Our study shows persistence of symptoms in a third of ambulatory patients 30 to 45 days after diagnosis even if we assume that those lost to follow-up were all asymptomatic. Fatigue, dyspnea, and loss of taste or smell were the main persistent symptoms. These results are in line with a recent study of 274 participants that reported the persistence of symptoms 14 to 21 days after diagnosis.

Transmission / Infection Control

26. **Absence of SARS-CoV-2 Transmission from Children in Isolation to Guardians, South Korea.** Lee EJ, Kim DH, Chang SH, et al. *Emerg Infect Dis*. 2020 Nov 30;27(1). doi: 10.3201/eid2701.203450. https://wwwnc.cdc.gov/eid/article/27/1/20-3450_article
Findings: We explored transmission of severe acute respiratory syndrome coronavirus 2 among 12 children and their uninfected guardians in hospital isolation rooms in South Korea. We found

that, even with close frequent contact, guardians who used appropriate personal protective equipment were not infected by children with diagnosed coronavirus disease.

27. Safety in the practice of decontaminating filtering facepiece respirators: A systematic review.

Gnatta JR, de Souza RQ, Lemos CS, et al. *Am J Infect Control*. 2020 Dec 3:S0196-6553(20)31032-4. doi: 10.1016/j.ajic.2020.11.022. [https://www.ajicjournal.org/article/S0196-6553\(20\)31032-4/fulltext](https://www.ajicjournal.org/article/S0196-6553(20)31032-4/fulltext)

Findings: The disinfectant/sterilizing agents most frequently tested at different concentrations and exposure periods were ultraviolet irradiation, vaporized hydrogen peroxide and steam sterilization. Microbial reduction was assessed in 21 (52.5%) studies. The only disinfectants/sterilizers that did not caused degradation of the material-integrity were alcohol, electric cooker, ethylene oxide and peracetic acid fogging. Exposure to ultraviolet irradiation or microwave generated-steam resulted in a non-significant reduction in filter performance. There is a complex relationship between the FFR raw materials and the cycle conditions of the decontamination methods, evidencing the need for validating FFRs by models and manufacturers, as well as the process. Some methods may require additional tests to demonstrate the safety of FFRs for use due to toxicity.

Vaccine

28. Durability of Responses after SARS-CoV-2 mRNA-1273 Vaccination. Widge AT et al. *N Engl J*

Med. 2020 Dec 3 doi: 10.1056/NEJMc2032195

https://www.nejm.org/doi/full/10.1056/NEJMc2032195?query=featured_home

Findings: We recently reported the results of a phase 1 trial of a messenger RNA vaccine, mRNA-1273, to prevent infection with SARS-CoV-2; those interim results covered a period of 57 days after the first vaccination. Here, we describe immunogenicity data 119 days after the first vaccination (90 days after the second vaccination) in 34 healthy adult participants in the same trial who received two injections of vaccine at a dose of 100 µg. The injections were received 28 days apart. At the 100-µg dose, mRNA-1273 produced high levels of binding and neutralizing antibodies that declined slightly over time, as expected, but they remained elevated in all participants 3 months after the booster vaccination. Serum neutralizing antibodies continued to be detected in all the participants at day 119. At day 119, the binding and neutralizing GMTs exceeded the median GMTs in a panel of 41 controls who were convalescing from Covid-19, with a median of 34 days since diagnosis. No serious adverse events were noted in the trial, no prespecified trial-halting rules were met, and no new adverse events that were considered by the investigators to be related to the vaccine occurred after day 57.

29. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK.

Voysey M, Costa Clemens SA, Madhi SA, et al. *Lancet*. December 08, 2020

DOI:[https://doi.org/10.1016/S0140-6736\(20\)32661-1](https://doi.org/10.1016/S0140-6736(20)32661-1)

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)32661-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32661-1/fulltext)

Findings: Between April 23 and Nov 4, 2020, 23 848 participants were enrolled and 11 636 participants were included in the interim primary efficacy analysis. In participants who received

two standard doses, vaccine efficacy was 62.1% and in participants who received a low dose followed by a standard dose, efficacy was 90.0%. Overall vaccine efficacy across both groups was 70.4%. From 21 days after the first dose, there were ten cases hospitalised for COVID-19, all in the control arm; two were classified as severe COVID-19, including one death. There were 74 341 person-months of safety follow-up (median 3.4 months): 175 severe adverse events occurred in 168 participants, 84 events in the ChAdOx1 nCoV-19 group and 91 in the control group. Three events were classified as possibly related to a vaccine: one in the ChAdOx1 nCoV-19 group, one in the control group, and one in a participant who remains masked to group allocation. ChAdOx1 nCoV-19 has an acceptable safety profile and has been found to be efficacious against symptomatic COVID-19 in this interim analysis of ongoing clinical trials.

Whole Person Care

30. **Clinician Perspectives on Caring for Dying Patients During the Pandemic: A Mixed-Methods Study.** Cook DJ, Takaoka A, Hoad N, et al. *Ann Intern Med.* 2020 Dec 8. doi: 10.7326/M20-6943. <https://www.acpjournals.org/doi/10.7326/M20-6943>

Findings: Many barriers to end-of-life care arose because of infection control practices that mandated visiting restrictions and personal protective equipment, with attendant practical and psychological consequences. During hospitalization, family visits inside or outside the patient's room were possible for 36 patients (80.0%); 13 patients (28.9%) had virtual visits with a relative or friend. At the time of death, 20 patients (44.4%) had a family member at the bedside. Clinicians endeavored to prevent unmarked deaths by adopting advocacy roles to "fill the gap" of absent family and by initiating new and established ways to connect patients and relatives. Clinicians expressed their humanity through several intentional practices to preserve personalized, compassionate end-of-life care for dying hospitalized patients during the SARS-CoV-2 pandemic.

Women & Children

31. **Evaluation of Rooming-in Practice for Neonates Born to Mothers with Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Italy.** Ronchi A, Pietrasanta C, Zavattoni M, et al. *JAMA Pediatr.* 2020 Dec 7. doi: 10.1001/jamapediatrics.2020.5086. <https://jamanetwork.com/journals/jamapediatrics/fullarticle/2773311>

Findings: Mothers with SARS-CoV-2 infection were encouraged to practice rooming-in and breastfeeding under a standardized protocol to minimize the risk of viral transmission. Of the 62 neonates enrolled (25 boys), born to 61 mothers (median age, 32 years) was diagnosed as having SARS-CoV-2 infection at postbirth checks. In that case, rooming-in was interrupted on day 5 of life because of severe worsening of the mother's clinical condition. The neonate became positive for the virus on day 7 of life and developed transient mild dyspnea. Ninety-five percent of the neonates enrolled were breastfed. The findings of this cohort study provide evidence-based information on the management of mother-infant dyads in case of SARS-CoV-2 maternal infection suggesting that rooming-in and breastfeeding can be practiced in women who are able to care for their infants.

32. **Changes in Preterm Birth Phenotypes and Stillbirth at 2 Philadelphia Hospitals During the SARS-CoV-2 Pandemic, March-June 2020.** Handley SC, Mullin AM, Elovitz MA, et al. *JAMA*. December 7, 2020. doi:10.1001/jama.2020.20991

<https://jamanetwork.com/journals/jama/fullarticle/2774087?resultClick=1>

Findings: We examined a diverse urban cohort in the US to determine if preterm birth, spontaneous preterm birth, medically indicated preterm birth, and stillbirth rates have changed during the SARS-CoV-2 pandemic. This study did not detect significant changes in preterm or stillbirth rates during the SARS-CoV-2 pandemic in a racially diverse urban cohort from 2 Philadelphia hospitals. Although these data allow for disaggregation of spontaneous and medically indicated preterm births, no differences in overall rates of these phenotypes were detected. These findings differ from a Danish report of decreasing preterm birth rates² and higher stillbirth rates in a UK hospital⁴ during the pandemic. The differences between studies may be due to differences in enforcement of lockdown orders, population heterogeneity, access to health care, or societal stressors.

*see also: [Stillbirths During the COVID-19 Pandemic in England, April-June 2020](#). Stowe J, Smith H, Thurland K, et al. *JAMA*. December 7, 2020. doi:10.1001/jama.2020.21369

33. **Arteritis and Large Vessel Occlusive Strokes in Children Following COVID-19 Infection.** Appavu B, Deng D, Dowling MM, et al. *Pediatrics*. 2020 Dec 4:e2020023440. doi: 10.1542/peds.2020-023440.

<https://pediatrics.aappublications.org/content/pediatrics/early/2020/12/02/peds.2020-023440.full.pdf>

We describe two previously healthy children that suffered disabling arterial ischemic strokes due to acute intracranial large vessel occlusion within 3-4 weeks of COVID-19 infection. Both children presented from communities with high COVID-19 case rates in the Southwest United States. An 8-year-old Native American female experienced severe iron deficiency anemia requiring blood transfusion and then presented with bilateral middle cerebral artery distribution strokes three weeks later. She underwent emergent mechanical thrombectomy of the left middle cerebral artery with successful clot retrieval but then experienced re-occlusion of that artery 5 hours after intervention. She also had evidence of cerebral arteritis on catheter angiography and vessel wall imaging, and clot pathology revealed recently formed, unorganized platelet and fibrin rich thrombus with sparse clusters of erythrocytes, degenerated histiocytes, few eosinophils and rare neutrophils. A 16-year old African American male demonstrated evidence of arteritis on brain magnetic resonance angiography and serological markers of cardiac and renal injury accompanied by positive lupus anticoagulant antibodies. The children described in this report express clinical features inconsistent with focal cerebral arteriopathy (FCA), including elevated markers of systemic inflammation in both, bilateral middle cerebral artery strokes in one case and multiple organ system dysfunction in the other case. Neither patient fulfilled criteria for multisystem inflammatory syndrome in children (MIS-C) given absence of fever. These cases illustrate that systemic post-infectious arteritis with cerebrovascular involvement may complicate COVID-19 infection in previously healthy school age children, and their presentations may overlap though not fulfill criteria for MIS-C or FCA.

GUIDELINES & CONSENSUS STATEMENTS

[Summary of Guidance for Public Health Strategies to Address High Levels of Community Transmission of SARS-CoV-2 and Related Deaths, December 2020.](#) Honein MA, Christie A, Rose DA, et al. *MMWR Morb Mortal Wkly Rep.* ePub: 4 December 2020. DOI: <http://dx.doi.org/10.15585/mmwr.mm6949e2>

[American College of Rheumatology Clinical Guidance for Pediatric Patients with Multisystem Inflammatory Syndrome in Children \(MIS-C\) Associated with SARS-CoV-2 and Hyperinflammation in COVID-19. Version 2.](#) Henderson LA, Canna SW, Friedman KG, et al. *Arthritis Rheumatol.* 2020 Dec 5. doi: 10.1002/art.41616.

[Canadian Internal Medicine Ultrasound \(CIMUS\) Expert Consensus Statement on the Use of Lung Ultrasound for the Assessment of Medical Inpatients With Known or Suspected Coronavirus Disease 2019.](#) Ma IWY, Hussain A, Wagner M, et al. *J Ultrasound Med.* 2020 Dec 4. doi: 10.1002/jum.15571.

FDA / CDC / NIH / WHO Updates

CDC - [Options to Reduce Quarantine for Contacts of Persons with SARS-CoV-2 Infection Using Symptom Monitoring and Diagnostic Testing](#)

CDC - [Domestic Travel During the COVID-19 Pandemic](#)

[FDA Analysis of Pfizer COVID-19 Vaccine Finds It Effective And Safe,](#) Dec 8, 2020.

[FDA Authorizes First COVID-19 and Flu Combination Test for use with home-collected samples,](#) Dec 4, 2020.

NIH COVID-19 Treatment Guidelines - [The COVID-19 Treatment Guidelines Panel’s Statement on the Emergency Use Authorization of the Casirivimab Plus Imdevimab Combination for the Treatment of COVID-19](#)

Commentary & News Releases

[Controversies in airway management of COVID-19 patients: updated information and international expert consensus recommendations.](#) Wei H, Jiang B, Behringer EC, et al. *Br J Anaesth.* 2020 Nov 6:S0007-0912(20)30896-5. doi: 10.1016/j.bja.2020.10.029.

[Pfizer and BioNTech Achieve First Authorization in the World for a Vaccine to Combat COVID-19](#)

New York Times: [Moderna Plans to Begin Testing Its Coronavirus Vaccine in Children](#)

[Therapy for Early COVID-19: A Critical Need.](#) Kim PS, Read SW, Fauci AS, *JAMA*. 2020;324(21):2149-2150. doi:10.1001/jama.2020.22813

[Definitions for COVID-19 reinfection, relapse and PCR re-positivity.](#) Yahav D, Yelin D, Eckerle I, et al. *Clin Microbiol Infect*. 2020 Dec 4:S1198-743X(20)30724-2. doi: 10.1016/j.cmi.2020.11.028.

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