

COVID-19 Resource Desk

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New Research

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Basic Science / Virology / Pre-clinical

1. **Genetic mechanisms of critical illness in Covid-19.** Pairo-Castineira, E, Clohisey, S, Klaric, L et al. *Nature* (2020). <https://doi.org/10.1038/s41586-020-03065-y>
<https://www.nature.com/articles/s41586-020-03065-y>
Findings: Host-mediated lung inflammation is present, and drives mortality, in critical illness caused by Covid-19. Host genetic variants associated with critical illness may identify mechanistic targets for therapeutic development. Here we report the results of the GenOMICC (Genetics Of Mortality In Critical Care) genome-wide association study (GWAS) in 2244 critically ill Covid-19 patients from 208 UK intensive care units (ICUs). Using Mendelian randomisation we found evidence in support of a causal link from low expression of IFNAR2, and high expression of TYK2, to life-threatening disease; transcriptome-wide association in lung tissue revealed that high expression of the monocyte/macrophage chemotactic receptor CCR2 is associated with severe Covid-19. Our results identify robust genetic signals relating to key host antiviral defence mechanisms, and mediators of inflammatory organ damage in Covid-19. Both mechanisms may be amenable to targeted treatment with existing drugs. Large-scale randomised clinical trials will be essential before any change to clinical practice.

Clinical Syndrome

2. **Incidence, clinical characteristics, risk factors and outcomes of Guillain-Barré syndrome in patients with Covid-19.** Fragiel M, Miró Ò, Llorens P, et al. *Ann Neurol*. 2020 Dec 9. doi: 10.1002/ana.25987. <https://onlinelibrary.wiley.com/doi/10.1002/ana.25987>
Findings: We diagnosed 11 GBS cases among 71,904 COVID patients attended at 61 Spanish emergency departments (ED) during the 2-month pandemic peak. The relative frequency of GBS among ED patients was higher in COVID (0.15%) than non-COVID (0.02%) patients as was the standardized incidence (9.44 and 0.69 cases/100,000-year, respectively). Regarding clinical characteristics, olfactory-gustatory disorders were more frequent in COVID-GBS than non-COVID-GBS and COVID-GBS patients. Although COVID-GBS patients were more frequently admitted to intensive care, mortality was not increased versus control groups. Our results suggest SARS-CoV-2 could be another viral infection causing GBS.

***see also: [Epidemiological and cohort study finds no association between COVID-19 and Guillain-Barré syndrome.](#)** Keddie S, Pakpoor J, Mousele C, et al. *Brain*. 2020 Dec 14:awaa433. doi: 10.1093/brain/awaa433.

- 3. Identification of distinct immunophenotypes in critically-ill COVID-19 patients.** Dupont T, Caillat-Zucman S, Fremeaux-Bacchi V, et al. *Chest*. 2020 Dec 11:S0012-3692(20)35351-4. doi: 10.1016/j.chest.2020.11.049.
<https://www.sciencedirect.com/science/article/pii/S0012369220353514?via%3Dihub>
Findings: We found that patients were distributed in three clusters bearing distinct immunologic features and associated to different ICU outcomes. Cluster 1 had a "humoral immunodeficiency" phenotype with predominant B-lymphocyte defect, relative hypogammaglobulinemia, and moderate inflammation. Cluster 2 had a "hyperinflammatory" phenotype, with high cytokine levels (IL-6, IL-1 β , IL-8, TNF α) associated to CD4+ and CD8+ T-lymphocyte defects. Cluster 3 had a "complement-dependent" phenotype with terminal complement activation markers (elevated C3 and sC5b-9). Severe COVID-19 patients exhibiting cytokine release marks, complement activation or B-lymphocyte defects are distinct from each other. Such immunologic variability argues in favor of targeting different mediators in different groups of patients and could serve as a basis for patient identification and clinical trial eligibility.

Diagnosics & Screening

- 4. Assessment of an Online Tool to Simulate the Effect of Pooled Testing for SARS-CoV-2 Detection in Asymptomatic and Symptomatic Populations.** Polage CR, Lee MJ, Hubbard C, et al. *JAMA Netw Open*. 2020 Dec 1;3(12):e2031517. doi: 10.1001/jamanetworkopen.2020.31517.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2773967>
Policy makers are promoting pooled testing as a strategy to increase the number of people tested for SARS-CoV-2 during the COVID-19 pandemic, especially for population screening. However, combining samples before testing brings trade-offs, such as decreasing the sensitivity and increasing the complexity of testing, that should be considered. We created an online tool using actual SARS-CoV-2 virus copy number (VCN) data—the COVID19 Pool Tool—to help policy makers understand how pooled testing compares with single-sample testing in different populations. Pooled testing can extend SARS-CoV-2 test supplies and increase the number of patients tested and cases detected, making it useful for population screening and resource-constrained settings. The complicated workflow, lower sensitivity for low-VCN patients, and need to repeat tests for positive pools are drawbacks. Sequential 2-stage pooling could reduce the burden of retesting from positive large pools.
- 5. Detection of SARS-CoV-2 N-antigen in blood during acute COVID-19 provides a sensitive new marker and new testing alternatives.** Hingrat QL, Visseaux B, Laouenan C, et al. *Clin Microbiol Infect*. 2020 Dec 8:S1198-743X(20)30721-7. doi: 10.1016/j.cmi.2020.11.025.
[https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(20\)30721-7/fulltext](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30721-7/fulltext)
Findings: This is the first evaluation of a commercially available serum N-antigen detection assay. It presents a robust specificity and sensitivity within the first 14 days after symptoms onset. Specificity was 98.4%. Sensitivity was 79.3% overall and 93.0% within 14 days after

symptoms onset. This approach provides a valuable new option for COVID-19 diagnosis, only requiring a blood draw and easily scalable in all clinical laboratories.

Epidemiology & Public Health

6. **Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic.** Buss LF, Prete CA Jr, Abraham CMM, et al. *Science*. 2020 Dec 8:eabe9728. doi: 10.1126/science.abe9728.
<https://science.sciencemag.org/content/early/2020/12/07/science.abe9728>
Findings: SARS-CoV-2 spread rapidly in the Brazilian Amazon and the attack rate there is an estimate of the final size of a largely unmitigated epidemic. We use a convenience sample of blood donors to show that by June, one month after the epidemic peak in Manaus, capital of Amazonas state, 44% of the population had detectable IgG antibodies. Correcting for cases without a detectable antibody response and antibody waning, we estimate a 66% attack rate in June, rising to 76% in October. This is higher than in São Paulo, in southeastern Brazil, where the estimated attack rate in October is 29%. These results confirm that, when poorly controlled, COVID-19 can infect a high fraction of the population causing high mortality.
7. **Analyses of Risk, Racial Disparity, and Outcomes among US Patients with Cancer and COVID-19 Infection.** Wang Q, Berger NA, Xu R, *JAMA Oncol*. December 10, 2020.
doi:10.1001/jamaoncol.2020.6178
Findings: In this case-control analysis of electronic medical records from 73.4 million unique patients, patients with a recent diagnosis of cancer were at significantly increased risk for COVID-19 infection and its adverse outcomes, especially in African Americans. Based on these findings, it is important to closely monitor patients with cancer and protect them from exposure to severe acute respiratory syndrome coronavirus 2 and the severe outcomes of COVID-19.
8. **SARS-CoV-2 infection and transmission in educational settings: a prospective, cross-sectional analysis of infection clusters and outbreaks in England.** Ismail SA, Saliba V, Lopez Bernal J, Ramsay ME, Ladhani SN. *Lancet Infect Dis*. 2020 Dec 8:S1473-3099(20)30882-3. doi: 10.1016/S1473-3099(20)30882-3.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30882-3/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30882-3/fulltext)
FINDINGS: A median of 38 000 early years settings, 15 600 primary schools, and 4000 secondary schools were open each day, with a median daily attendance of 928 000 students overall. There were 113 single cases of SARS-CoV-2 infection, nine coprimary cases, and 55 outbreaks. The risk of an outbreak increased by 72% for every five cases per 100 000 population increase in community incidence. Staff had higher incidence than students (27 cases per 100 000 per day among staff compared with 18 cases in early years students, 6·0 cases in primary schools students, and 6·8 cases in secondary school students]), and most cases linked to outbreaks were in staff members (154 [73%] staff vs 56 [27%] children of 210 total cases). Probable direction of transmission was staff to staff in 26 outbreaks, staff to student in eight outbreaks, student to staff in 16 outbreaks, and student to student in five outbreaks. SARS-CoV-2 infections and outbreaks were uncommon in educational settings during the summer half-term

in England. The strong association with regional COVID-19 incidence emphasises the importance of controlling community transmission to protect educational settings. Interventions should focus on reducing transmission in and among staff.

9. **COVID-19 Mortality among American Indian and Alaska Native Persons — 14 States, January–June 2020.** Arrazola J, Masiello MM, Joshi S, et al. *MMWR Morb Mortal Wkly Rep* 2020;69:1853–1856. DOI: <http://dx.doi.org/10.15585/mmwr.mm6949a3>
https://www.cdc.gov/mmwr/volumes/69/wr/mm6949a3.htm?s_cid=mm6949a3_w
Findings: COVID-19 incidence is higher among American Indians/Alaska Natives (AI/ANs) than among non-Hispanic Whites. In 2009, AI/ANs experienced disproportionately high pandemic influenza A(H1N1)–associated mortality. Based on data from 14 participating states, age-adjusted COVID-19–associated mortality among AI/ANs was 1.8 times that among non-Hispanic Whites. Among AI/ANs, mortality was higher among men than among women, and the disparity in mortality compared with non-Hispanic Whites was highest among persons aged 20–49 years. AI/ANs have experienced disproportionate rates of infection and mortality during the COVID-19 pandemic. The excess risk, especially for AI/AN males and persons aged 20–49 years, should be considered when planning and implementing medical countermeasures and other prevention activities.

10. **Impact of Population Growth and Aging on Estimates of Excess U.S. Deaths during the COVID-19 Pandemic, March to August 2020.** Shiels MS, Almeida JS, García-Closas M, Albert PS, Freedman ND, de González AB. *Ann Intern Med.* 2020 Dec 15. doi: 10.7326/M20-7385.
<https://www.acpjournals.org/doi/10.7326/M20-7385>
Findings: From March through August 2020, 1,671,400 deaths were registered in the United States, including 173,300 COVID-19 deaths. An average of 1,370,000 deaths were reported over the same months during 2015 to 2019, for a crude excess of 301,400 deaths. However, the 2020 U.S. population includes 5.04 million more persons aged 65 years and older than the average population in 2015 to 2019 (a 10% increase). After population changes were taken into account, an estimated 217,900 excess deaths occurred from March through August 2020. Most excess non-COVID-19 deaths occurred in April, July, and August, and 34 900 (78%) were in persons aged 25 to 64 years. Diabetes, Alzheimer disease, and heart disease caused the most non-COVID-19 excess deaths. Conclusion: The COVID-19 pandemic resulted in an estimated 218,000 excess deaths in the United States between March and August 2020, and 80% of those deaths had COVID-19 as the underlying cause. Accounting for population changes substantially reduced the excess non-COVID-19 death estimates, providing important information for guiding future clinical and public health interventions.

11. **Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Blockers Use and COVID-19 Infection among 824,650 Patients with Hypertension from a US integrated Healthcare System.** An J, Wei R, Zhou H, et al. *J Am Heart Assoc.* 2020 Dec 14:e017773. doi: 10.1161/JAHA.120.019669. <https://www.ahajournals.org/doi/pdf/10.1161/JAHA.120.019669>
Findings: We identified patients with hypertension as of March 1, 2020 from Kaiser Permanente Southern California. Patients who received ACEIs, ARBs, calcium channel blocks (CCB), beta-blockers (BB), thiazide diuretics (TD), or no therapy were identified using outpatient pharmacy

data covering the index date. Among 824,650 patients with hypertension, 16,898 (2.0%) were tested for Covid-19. Of those tested, 1,794 (10.6%) had a positive result. Overall, exposure to ACEIs or ARBs was not statistically significantly associated with Covid-19 infection. The associations between ACEI use and Covid-19 infection varied in different age groups. ACEI use was associated with lower odds of Covid-19 among those aged ≥ 85 years. Use of no antihypertensive medication was significantly associated with increased odds of Covid-19 infection compared with CCB/BB/TD. Neither ACEI nor ARB use was associated with increased likelihood of Covid-19 infection. Decreased odds of Covid-19 infection among adults ≥ 85 years using ACEIs warrants further investigation.

Healthcare Delivery & Healthcare Workers

12. **Reliability and limits of transport-ventilators to safely ventilate severe patients in special surge situations.** Savary D, Lesimple A, Beloncle F, et al. *Ann Intensive Care*. 2020 Dec 9;10(1):166. doi: 10.1186/s13613-020-00782-5.
<https://annalsofintensivecare.springeropen.com/articles/10.1186/s13613-020-00782-5>
Findings: Two pneumatic transport ventilators, two turbine transport ventilators and an ICU ventilator were evaluated on a Michigan test lung. We tested each ventilator with different set volumes and compliances and a resistance of 15 cmH₂O/l/s based on values described in COVID-19 Acute Respiratory Distress Syndrome. In surge situations such as COVID-19 pandemic, transport ventilators may be used to accurately control delivered volumes in locations, where only oxygen pressure supply is available. Performances regarding triggering function are acceptable for three out of the four transport ventilators tested.
13. **Comparison of 2 Triage Scoring Guidelines for Allocation of Mechanical Ventilators.** Wunsch H, Hill AD, Bosch N, et al. *JAMA Netw Open*. 2020 Dec 1;3(12):e2029250. doi: 10.1001/jamanetworkopen.2020.29250.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/10.1001/jamanetworkopen.2020.29250>
Findings: Among 40 439 intensive care unit admissions of patients who received mechanical ventilation, the mean SOFA score was 4.5. Using the New York State triage criteria, 8.9% were in the lowest priority category. Using the White and Lo triage criteria, 4.3% were in the lowest priority category. Only 655 admissions (1.6%) were in the lowest priority category for both guidelines, with the κ statistic for agreement equal to 0.20. Use of 2 initially proposed ventilator triage guidelines identified approximately 1 in every 10 to 25 admissions as having the lowest priority for ventilator allocation, with little agreement. Clinical assessment of different potential criteria for triage decisions in critically ill populations is important to ensure valid and equitable allocation of resources.

Laboratory Results

14. **Functional SARS-CoV-2-Specific Immune Memory Persists after Mild COVID-19.** Rodda LB, Netland J, Shehata L, et al. *Cell*. 2020 Nov 23:S0092-8674(20)31565-8. doi:

10.1016/j.cell.2020.11.029.

<https://www.sciencedirect.com/science/article/pii/S0092867420315658>

Findings: Most SARS-CoV-2 infected individuals experience mildly symptomatic COVID-19, but it is unknown whether this can induce persistent immune memory that could contribute to immunity. We performed a longitudinal assessment of individuals recovered from mild COVID-19 to determine whether they develop and sustain multifaceted SARS-CoV-2-specific immunological memory. Recovered individuals developed SARS-CoV-2-specific immunoglobulin (IgG) antibodies, neutralizing plasma, and memory B and memory T cells that persisted for at least 3 months. Our data further reveal that SARS-CoV-2-specific IgG memory B cells increased over time. Additionally, SARS-CoV-2-specific memory lymphocytes exhibited characteristics associated with potent antiviral function: memory T cells secreted cytokines and expanded upon antigen re-encounter, whereas memory B cells expressed receptors capable of neutralizing virus when expressed as monoclonal antibodies. Therefore, mild COVID-19 elicits memory lymphocytes that persist and display functional hallmarks of antiviral immunity.

Prognosis

15. **Utility of established prognostic scores in COVID-19 hospital admissions: multicentre prospective evaluation of CURB-65, NEWS2 and qSOFA.** NW Collaborative Organisation for Respiratory Research. *BMJ Open Respir Res.* 2020 Dec;7(1):e000729. doi: 10.1136/bmjresp-2020-000729. <https://bmjopenrespres.bmj.com/content/7/1/e000729>
Findings: Data were collected for 830 people with COVID-19 admitted across seven hospitals. All scores underestimated mortality compared with pre-COVID-19 cohorts, and overall prognostic performance was generally poor. In the setting of COVID-19, existing prognostic scores underestimated risk. The design of new prognostic tools should focus on features of respiratory compromise rather than circulatory collapse. We provide a baseline set of variables which are relevant to COVID-19 outcomes and may be used as a basis for developing a bespoke COVID-19 prognostication tool.
16. **Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission.** Peckham, H., de Groot, N.M., Raine, C. et al. *Nat Commun* 11, 6317 (2020). <https://doi.org/10.1038/s41467-020-19741-6> <https://www.nature.com/articles/s41467-020-19741-6>
Findings: Here, we present a meta-analysis of 3,111,714 reported global cases to demonstrate that, whilst there is no difference in the proportion of males and females with confirmed COVID-19, male patients have almost three times the odds of requiring intensive treatment unit admission and higher odds of death compared to females. With few exceptions, the sex bias observed in COVID-19 is a worldwide phenomenon. An appreciation of how sex is influencing COVID-19 outcomes will have important implications for clinical management and mitigation strategies for this disease.
17. **Protracted viral shedding and viral load are associated with ICU mortality in Covid-19 patients with acute respiratory failure.** Bitker L, Dhelt F, Chauvelot L, et al. *Ann Intensive Care.* 2020

Dec 10;10(1):167. doi: 10.1186/s13613-020-00783-4.

<https://annalsofintensivecare.springeropen.com/articles/10.1186/s13613-020-00783-4>

Findings: 129 patients were included in the study, of whom 44 (34%) died in ICU. Viral load was significantly higher in patients deceased as compared to patients alive at ICU discharge. The median time to SARS-CoV-2 negativation on RT-PCR was 19 days in patients alive at ICU discharge and 26 days in non-survivors at ICU discharge. Viral load in respiratory samples is significantly lower and viral shedding significantly shorter in ICU survivors of COVID-19 associated acute respiratory failure. Protracted viral shedding is unrelated to occurrence of fibrosis on lung CT.

18. **Risk Factors Associated with In-Hospital Mortality in a US National Sample of Patients With COVID-19.** Rosenthal N, Cao Z, Gundrum J, Sianis J, Safo S. *JAMA Netw Open*. 2020 Dec 1;3(12):e2029058. doi: 10.1001/jamanetworkopen.2020.29058.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2773971>

Findings: Overall, 64 781 patients with COVID-19 (29 479 [45.5%] outpatients; 35 302 [54.5%] inpatients) were analyzed. The median age was 46 (33-59) years for outpatients and 65 (52-77) years for inpatients; 31 968 (49.3%) were men, 25 841 (39.9%) were White US residents, and 14 340 (22.1%) were Black US residents. In-hospital mortality was 20.3% among inpatients (7164 patients). A total of 5625 inpatients (15.9%) received invasive mechanical ventilation, and 6849 (19.4%) were admitted to the ICU. Median inpatient LOS was 6 days. Median ICU LOS was 5 days. In this cohort study of patients with COVID-19 infection in US acute care hospitals, COVID-19 was associated with high ICU admission and in-hospital mortality rates. Use of statins, angiotensin-converting enzyme inhibitors, and calcium channel blockers were associated with decreased odds of death. Understanding the potential benefits of unproven treatments will require future randomized trials.

19. **Readmission and Death after Initial Hospital Discharge Among Patients With COVID-19 in a Large Multihospital System.** Donnelly JP, Wang XQ, Iwashyna TJ, Prescott HC. *JAMA*. December 14, 2020. doi:10.1001/jama.2020.21465

<https://jamanetwork.com/journals/jama/fullarticle/2774380>

Findings: In this national cohort of VA patients, 27% of survivors of COVID-19 hospitalization were readmitted or died by 60 days after discharge, and this rate was lower than matched survivors of pneumonia or heart failure. However, rates of readmission or death were higher than pneumonia or heart failure during the first 10 days after discharge following COVID-19 hospitalization, suggesting a period of heightened risk of clinical deterioration. Study limitations include the inability to measure readmissions to non-VA hospitals and an older, male-predominant study population, which may be at higher risk of severe manifestations of COVID-19. Public health surveillance or clinical trials focused exclusively on inpatient mortality may substantially underestimate burdens of COVID-19.

20. **Risk factors associated with Covid-19-associated pulmonary aspergillosis in ICU patients: a French multicentric retrospective cohort.** Dellière S, Dudoignon E, Fodil S, et al. *Clin Microbiol Infect*. 2020 Dec 11:S1198-743X(20)30756-4. doi: 10.1016/j.cmi.2020.12.005.

<https://www.sciencedirect.com/science/article/pii/S1198743X20307564?via%3Dihub>

Findings: We conducted a retrospective cohort study including all successive COVID-19 patients hospitalized in four ICUs with secondary deterioration and ≥ 1 respiratory sample sent to the mycology department. Probable IPA was diagnosed in 21 out of the 366 COVID-19 patients (5.7%) admitted to the ICU and the 108 patients (19.4%) who underwent respiratory sampling for deterioration. No significant differences were observed between patients with and without IPA regarding age, gender, medical history and severity on admission and during hospitalization. Treatment with azithromycin for ≥ 3 days was associated with the diagnosis of probable IPA. A trend was observed with high dose dexamethasone and the occurrence of IPA. Overall mortality was higher in the IPA patients (15/21, 71.4% vs. 32/87, 36.8%; $p < 0.01$). IPA is a relatively frequent complication in severe COVID-19 patients responsible for increased mortality. Azithromycin, known to have immunomodulatory properties, may contribute to increase COVID-19 patient susceptibility to IPA.

21. **Metformin use is associated with a reduced risk of mortality in patients with diabetes hospitalised for COVID-19.** CORONADO investigators. *Diabetes Metab.* 2020 Dec 10:101216. doi: 10.1016/j.diabet.2020.101216.

<https://www.sciencedirect.com/science/article/pii/S1262363620302731?via%3Dihub>

Findings: Among the 2449 patients included, 1496 were metformin users and 953 were not. Compared with non-users, metformin users were younger with a lower prevalence of diabetic complications but had more severe features of COVID-19 on admission. The primary endpoint occurred in 28.0% of metformin users (vs 29.0% in non-users, $P = 0.6134$) on day 7 and in 32.6% (vs 38.7%, $P = 0.0023$) on day 28. The mortality rate was lower in metformin users on day 7 (8.2 vs 16.1%, $P < 0.0001$) and on day 28 (16.0 vs 28.6%, $P < 0.0001$). Metformin use appeared to be associated with a lower risk of death in patients with diabetes hospitalised for COVID-19.

Therapeutics

22. **Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19.** Kalil AC, Patterson TF, Mehta AK, Henry Arguinchona, et al. [PSJH author] *NEJM.* Dec 11, 2020. DOI: 10.1056/NEJMoa2031994

https://www.nejm.org/doi/full/10.1056/NEJMoa2031994?query=featured_home

Findings: A total of 1033 patients underwent randomization (with 515 assigned to combination treatment and 518 to control). Patients receiving baricitinib had a median time to recovery of 7 days, as compared with 8 days with control, and a 30% higher odds of improvement in clinical status at day 15. Patients receiving high-flow oxygen or noninvasive ventilation at enrollment had a time to recovery of 10 days with combination treatment and 18 days with control. The 28-day mortality was 5.1% in the combination group and 7.8% in the control group. Serious adverse events were less frequent in the combination group than in the control group. Baricitinib plus remdesivir was superior to remdesivir alone in reducing recovery time and accelerating improvement in clinical status among patients with Covid-19, notably among those receiving high-flow oxygen or noninvasive ventilation. The combination was associated with fewer serious adverse events.

23. **Corticosteroids in patients hospitalised for COVID-19 pneumonia who require oxygen: observational comparative study using routine care data.** COCORICO study Group, et al. *Clin Microbiol Infect.* 2020 Dec 7:S1198-743X(20)30731-X. doi: 10.1016/j.cmi.2020.11.035. [https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(20\)30731-X/fulltext](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30731-X/fulltext)
Findings: Among the 891 patients included in the analysis, 203 were assigned to the CTC group. Use of corticosteroids was not significantly associated with risk of intubation or death by day 28 or cumulative death rate. However, use of corticosteroids was associated with reduced risk of intubation or death by day 28 in the prespecified subgroups of patients requiring oxygen ≥ 3 L/min or C-reactive protein level ≥ 100 mg/L. Number of hyperglycaemia events was higher for patients with than without corticosteroids, but number of infections was similar. We found no association between the use of corticosteroids and intubation or death in the broad population of patients 18 to 80 years old with COVID-19 hospitalized in non-intensive care unit settings. However, the treatment was associated with reduced risk of intubation or death for patients with ≥ 3 L/min oxygen or C-reactive protein level ≥ 100 mg/L at baseline. Further research need to confirm the right timing of corticosteroids for patients with COVID-19 requiring oxygen only.
24. **Corticosteroid therapy is associated with improved outcome in critically ill COVID-19 patients with hyperinflammatory phenotype.** Chen H, Xie J, Su N, et al. *Chest.* 2020 Dec 11:S0012-3692(20)35352-6. doi: 10.1016/j.chest.2020.11.050. <https://www.sciencedirect.com/science/article/pii/S0012369220353526?via%3Dihub>
Findings: Critically ill patients with COVID-19 from Tongji hospital between Jan 2020 and Feb 2020 were included, and the main exposure of interest was the administration of intravenous corticosteroids. A total of 428 patients were included, and 280/428 (65.4%) patients received corticosteroid therapy. Our analysis identified two phenotypes of COVID-19, and compared to the hypoinflammatory phenotype, the hyperinflammatory phenotype was characterized by elevated levels of proinflammatory cytokines, higher SOFA scores and higher rates of complications. Corticosteroid therapy was associated with a reduced 28-day mortality in patients with hyperinflammatory phenotype.
25. **Use of Intravenous Immunoglobulin (Prevagen or Octagam) for the Treatment of COVID-19: Retrospective Case Series.** Herth FJF, Sakoulas G, Haddad F. *Respiration.* 2020 Dec 14:1-9. doi: 10.1159/000511376. <https://www.karger.com/Article/FullText/511376>
Findings: We retrospectively evaluated the clinical courses of 12 COVID-19 patients who received IVIG at various stages of their illness, including within the first 72 h of clinical presentation, after initiation of mechanical ventilation, and after prolonged ventilation and ICU stay. The patients included 9 men and 3 women with a median age of 50 years (range 23-74). The IVIG total dose ranged from 0.5 to 2.0 g/kg (median 1.25 g/kg) distributed over 1-4 daily doses. The most common regimen received was 0.5 g/kg daily for 3 days. The median time to IVIG administration was 9 days (range 0-48 days) after admission. The median time from first IVIG dose administration to hospital discharge was 14 days (range 3-48). The 5 patients who received IVIG ≤ 4 days of admission demonstrated a significantly shorter length of hospital stay after treatment (median 7 days, range 3-14 days) than the 7 patients who received it >7 days after admission (median 33 days, range 8-48 days, $p = 0.03$, Mann-Whitney U test). These cases demonstrate that IVIG may improve the clinical state of patients with moderate to severe

COVID-19 infection. Despite very high illness severity scores, all patients survived hospital discharge. No thrombotic events occurred and IVIG was well tolerated, despite most cases demonstrating very elevated D-dimer suggestive of active intravascular fibrinolysis. We believe that IVIG warrants immediate clinical trial evaluation in COVID-19 to confirm its role as a mainstay treatment of moderate to severe COVID-19 infection as a means to reduce hospital stay and utilization of ICU resources, including mechanical ventilation, and potentially reduce mortality.

26. Azithromycin in Hospitalised Patients with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. Horby PW, Roddick A, Spata E, et al. *medRxiv PREPRINT*. doi: <https://doi.org/10.1101/2020.12.10.20245944>

Findings: Azithromycin has been proposed as a treatment for COVID-19 on the basis of its immunomodulatory actions. We evaluated the efficacy and safety of azithromycin in hospitalised patients with COVID-19. In this randomised, controlled, open-label, adaptive platform trial, several possible treatments were compared with usual care in patients hospitalised with COVID-19 in the UK. Eligible and consenting patients were randomly allocated to either usual standard of care alone or usual standard of care plus azithromycin 500 mg once daily by mouth or intravenously for 10 days or until discharge (or one of the other treatment arms). Overall, 496 (19%) patients allocated to azithromycin and 997 (19%) patients allocated to usual care died within 28 days. Consistent results were seen in all pre-specified subgroups of patients. There was no difference in duration of hospitalisation (median 12 days vs. 13 days) or the proportion of patients discharged from hospital alive within 28 days (60% vs. 59%). Among those not on invasive mechanical ventilation at baseline, there was no difference in the proportion meeting the composite endpoint of invasive mechanical ventilation or death (21% vs. 22%). Interpretation: In patients hospitalised with COVID-19, azithromycin did not provide any clinical benefit. Azithromycin use in patients hospitalised with COVID-19 should be restricted to patients where there is a clear antimicrobial indication.

Transmission / Infection Control

27. Evaluation of Cloth Masks and Modified Procedure Masks as Personal Protective Equipment for the Public during the COVID-19 Pandemic. Clapp PW, Sickbert-Bennett EE, Samet JM, et al. *JAMA Intern Med*. December 10, 2020. doi:10.1001/jamainternmed.2020.8168 <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2774266>

Findings: 7 consumer-grade masks and 5 medical procedure mask modifications were fitted on an adult male volunteer, and FFE measurements were collected. The consumer-grade masks tested included (1) a 2-layer woven nylon mask with ear loops, (2) a cotton bandana folded diagonally once (ie, “bandit” style) or in a (3) multilayer rectangle according to the instructions presented by the US Surgeon General, (4) a single-layer woven polyester/nylon mask with ties, (5) a nonwoven polypropylene mask with fixed ear loops, (6) a single-layer woven polyester gaiter/neck cover balaclava bandana, and (7) a 3-layer woven cotton mask with ear loops. Medical procedure mask modifications included (1) tying the mask’s ear loops and tucking in the side pleats, (2) fastening ear loops behind the head with 3-dimensional–printed ear guards, (3) fastening ear loops behind the head with a claw-type hair clip, (4) enhancing the mask/face

seal with rubber bands over the mask, and (5) enhancing the mask/face seal with a band of nylon hosiery over the fitted mask. The mean (SD) FFE of consumer grade masks tested on 1 adult male with no beard ranged from 79.0% to 26.5%, with the 2-layer woven nylon mask having the highest FFE. While modifications to improve medical procedure mask fit can enhance the filtering capability and reduce inhalation of airborne particles, this study demonstrates that the FFEs of consumer-grade masks available to the public are, in many cases, nearly equivalent to or better than their non-N95 respirator medical mask counterparts.

28. **Household Transmission of SARS-CoV-2: A Systematic Review and Meta-analysis.** Madewell ZJ, Yang Y, Longini IM Jr, et al. *JAMA Netw Open.* 2020 Dec 1;3(12):e2031756. doi: 10.1001/jamanetworkopen.2020.31756
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/10.1001/jamanetworkopen.2020.31756>

Findings: A total of 54 relevant studies with 77 758 participants reporting household secondary transmission were identified. Estimated household secondary attack rate was 16.6%, higher than secondary attack rates for SARS-CoV and MERS-CoV. Household secondary attack rates were increased from symptomatic index cases than from asymptomatic index cases, to adult contacts than to child contacts, to spouses than to other family contacts, and in households with 1 contact than in households with 3 or more contacts. The findings of this study suggest that given that individuals with suspected or confirmed infections are being referred to isolate at home, households will continue to be a significant venue for transmission of SARS-CoV-2.

29. **Towards an accurate and systematic characterisation of persistently asymptomatic infection with SARS-CoV-2.** Meyerowitz EA, Richterman A, Bogoch II, et al. *Lancet Infect Dis.* 2020 Dec 7:S1473-3099(20)30837-9. doi: 10.1016/S1473-3099(20)30837-9.

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30837-9/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30837-9/fulltext)

Findings: People with persistently asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection experience no symptoms throughout the course of infection, and pre-symptomatic individuals become infectious days before they report symptoms. Transmission of SARS-CoV-2 from individuals without symptoms contributes to pandemic spread, but the extent of transmission from persistently asymptomatic individuals remains unknown. We describe three methodological issues that hinder attempts to estimate this proportion. First, incomplete symptom assessment probably overestimates the asymptomatic fraction. Second, studies with inadequate follow-up misclassify pre-symptomatic individuals. Third, serological studies might identify people with previously unrecognised infection, but reliance on poorly defined antibody responses and retrospective symptom assessment might result in misclassification. We provide recommendations regarding definitions, detection, documentation, and follow-up to improve the identification and evaluation of people with persistently asymptomatic SARS-CoV-2 infection and their contacts. Accurate characterisation of the persistently asymptomatic fraction of infected individuals might shed light on COVID-19 pathogenesis and transmission dynamics and inform public health responses.

30. **Efficacy of commercial mouth-rinses on SARS-CoV-2 viral load in saliva: randomized control trial in Singapore.** Seneviratne CJ, Balan P, Ko KKK, et al. *Infection*. 2020 Dec 14. doi: 10.1007/s15010-020-01563-9. <https://link.springer.com/article/10.1007/s15010-020-01563-9>
Findings: A total of 36 SARS-CoV-2-positive patients were recruited, of which 16 patients were randomly assigned to four groups-PI group (n = 4), CHX group (n = 6), CPC group (n = 4) and water as control group (n = 2). Saliva samples were collected from all patients at baseline and at 5 min, 3 h and 6 h post-application of mouth-rinses/water. The samples were subjected to SARS-CoV-2 RT-PCR analysis. The effect of decreasing salivary load with CPC and PI mouth-rinsing was observed to be sustained at 6 h time point. Within the limitation of the current study, as number of the samples analyzed, the use of CPC and PI formulated that commercial mouth-rinses may be useful as a pre-procedural rinse to help reduce the transmission of COVID-19.
31. **Assessment of the risk of SARS-CoV-2 reinfection in an intense re-exposure setting.** Abu-Raddad LJ, Chemaitelly H, Malek JA, et al. *Clin Infect Dis*. 2020 Dec 14:ciaa1846. doi: 10.1093/cid/ciaa1846. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1846/6033728>
Findings: Out of 133,266 laboratory-confirmed SARS-CoV-2 cases, 243 persons (0.18%) had at least one subsequent positive swab \geq 45 days after the first-positive swab. Of these, 54 cases (22.2%) had strong or good evidence for reinfection. Median time between first and reinfection swab was 64.5 days (range: 45-129). SARS-CoV-2 reinfection can occur but is a rare phenomenon suggestive of protective immunity against reinfection that lasts for at least a few months post primary infection.

Vaccine

32. **The Advisory Committee on Immunization Practices' Interim Recommendation for Allocating Initial Supplies of COVID-19 Vaccine - United States, 2020.** Dooling K, McClung N, Chamberland M, et al. *MMWR Morb Mortal Wkly Rep*. 2020 Dec 11;69(49):1857-1859. doi: 10.15585/mmwr.mm6949e1. <https://www.cdc.gov/mmwr/volumes/69/wr/mm6949e1.htm>
Findings: The Advisory Committee on Immunization Practices (ACIP) advises CDC on population groups and circumstances for vaccine use. ACIP convened on December 1, 2020, in advance of the completion of FDA's review of the Emergency Use Authorization application, to provide interim guidance to federal, state, and local jurisdictions on allocation of initial doses of COVID-19 vaccine. ACIP recommended that, when a COVID-19 vaccine is authorized by FDA and recommended by ACIP, both 1) health care personnel and 2) residents of long-term care facilities (LTCFs) be offered vaccination in the initial phase of the COVID-19 vaccination program. In its deliberations, ACIP considered scientific evidence of SARS-CoV-2 epidemiology, vaccination program implementation, and ethical principles. The interim recommendation might be updated over the coming weeks based on additional safety and efficacy data from phase III clinical trials and conditions of FDA Emergency Use Authorization.

33. **Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine.** Polack FP, Thomas SJ, Kitchin N, et al. *N Engl J Med.* 2020 Dec 10. doi: 10.1056/NEJMoa2034577.

<https://www.nejm.org/doi/full/10.1056/NEJMoa2034577>

Findings: In an ongoing multinational, placebo-controlled, observer-blinded, pivotal efficacy trial, we randomly assigned persons 16 years of age or older in a 1:1 ratio to receive two doses, 21 days apart, of either placebo or the BNT162b2 vaccine candidate (30 µg per dose). BNT162b2 is a lipid nanoparticle-formulated, nucleoside-modified RNA vaccine that encodes a prefusion stabilized, membrane-anchored SARS-CoV-2 full-length spike protein. The primary end points were efficacy of the vaccine against laboratory-confirmed Covid-19 and safety. A total of 43,548 participants underwent randomization, of whom 43,448 received injections: 21,720 with BNT162b2 and 21,728 with placebo. There were 8 cases of Covid-19 with onset at least 7 days after the second dose among participants assigned to receive BNT162b2 and 162 cases among those assigned to placebo; BNT162b2 was 95% effective in preventing Covid-19 (95% credible interval, 90.3 to 97.6). Similar vaccine efficacy (generally 90 to 100%) was observed across subgroups defined by age, sex, race, ethnicity, baseline body-mass index, and the presence of coexisting conditions. Among 10 cases of severe Covid-19 with onset after the first dose, 9 occurred in placebo recipients and 1 in a BNT162b2 recipient. The safety profile of BNT162b2 was characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache. The incidence of serious adverse events was low and was similar in the vaccine and placebo groups. CONCLUSIONS: A two-dose regimen of BNT162b2 conferred 95% protection against Covid-19 in persons 16 years of age or older. Safety over a median of 2 months was similar to that of other viral vaccines.

34. **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.**

Oxford COVID Vaccine Trial Group. *Lancet.* 2020 Dec 8:S0140-6736(20)32661-1. doi: 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: This analysis includes data from four ongoing blinded, randomised, controlled trials done across the UK, Brazil, and South Africa. Participants aged 18 years and older were randomly assigned (1:1) to ChAdOx1 nCoV-19 vaccine or control (meningococcal group A, C, W, and Y conjugate vaccine or saline). Participants in the ChAdOx1 nCoV-19 group received two doses containing 5×10^{10} viral particles (standard dose; SD/SD cohort); a subset in the UK trial received a half dose as their first dose (low dose) and a standard dose as their second dose (LD/SD cohort). Between April 23 and Nov 4, 2020, 23 848 participants were enrolled and 11 636 participants (7548 in the UK, 4088 in Brazil) 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.

Women & Children

35. **Factors Associated with Severe SARS-CoV-2 Infection.** Ouldali N, Yang DD, Madhi F. et al. *Pediatrics*. December 2020, e2020023432; DOI: <https://doi.org/10.1542/peds.2020-023432>
Findings: We conducted a French national prospective surveillance of children hospitalized with SARS-CoV-2 infection. We included all children with confirmed SARS-CoV-2 infection in sixty hospitals during February 15 to June 1, 2020. The main outcome was the proportion of children with severe disease, defined by hemodynamic or ventilatory (invasive or not) support requirement. We included 397 hospitalized children with SARS-CoV-2 infection. We identified several clinical patterns, ranging from pauci-symptomatic children, admitted for surveillance, to lower respiratory tract infection or Multisystem Inflammatory Syndrome in Children. Children <90 days old accounted for 37% of cases (145/397), but only 4 (3%) had severe disease. Excluding children with MIS-C (n=29) and hospitalized for a diagnosis not related to SARS-CoV-2 (n=62), 23/306 (11%) children had severe disease, including 6 deaths. Factors independently associated with severity were age ≥ 10 years (OR=3.4, 95% CI [1.1; 10.3]), hypoxemia (OR=8.9 [2.6; 29.7]), CRP ≥ 80 mg/L (OR=6.6 [1.4; 27.5]). In contrast with preliminary reports, young age was not independent factor associated with severe SARSCoV-2 infection, and children <90 days old were at the lowest risk of severe disease evolution. This may help physicians to better identify risk of severe disease progression in children
36. **Mucocutaneous Manifestations of Multisystem Inflammatory Syndrome in Children during the COVID-19 Pandemic.** Young TK, Shaw KS, Shah JK, et al. *JAMA Dermatol*. 2020 Dec 9. doi: 10.1001/jamadermatol.2020.4779.
<https://jamanetwork.com/journals/jamadermatology/fullarticle/2773994>
Findings: Twenty-five children (11 girls [44%]; median age, 3 years) were identified who met definitional criteria for MIS-C; an additional 10 children (5 girls [50%]; median age, 1.7 years) were included as probable MIS-C cases. Of the 35 patients, 29 (83%) exhibited mucocutaneous changes, with conjunctival injection (n = 21), palmoplantar erythema (n = 18), lip hyperemia (n = 17), periorbital erythema and edema (n = 7), strawberry tongue (n = 8), and malar erythema (n = 6) being the most common findings. Recognition of mucocutaneous findings occurred a mean of 2.7 days after the onset of fever. The duration of mucocutaneous findings varied from hours to days (median duration, 5 days). Neither the presence nor absence of mucocutaneous findings was significantly associated with overall disease severity. In this case series of hospitalized children with suspected MIS-C during the COVID-19 pandemic, a wide spectrum of mucocutaneous findings was identified. Despite their protean and transient nature, these mucocutaneous features serve as important clues in the recognition of MIS-C.
37. **Evidence of thrombotic microangiopathy in children with SARS-CoV-2 across the spectrum of clinical presentations.** Diorio C, McNerney KO, Lambert M, et al. *Blood Adv*. 2020 Dec 8;4(23):6051-6063. doi: 10.1182/bloodadvances.2020003471.

<https://ashpublications.org/bloodadvances/article/4/23/6051/474421/Evidence-of-thrombotic-microangiopathy-in-children>

Findings: We enrolled 50 hospitalized pediatric patients with acute SARS-CoV-2 infection (n = 21, minimal coronavirus disease 2019 [COVID-19]; n = 11, severe COVID-19) or MIS-C (n = 18). A high proportion of tested children with SARS-CoV-2 infection had evidence of complement activation and met clinical and diagnostic criteria for TMA. Future studies are needed to determine if hospitalized children with SARS-CoV-2 should be screened for TMA, if TMA-directed management is helpful, and if there are any short- or long-term clinical consequences of complement activation and endothelial damage in children with COVID-19 or MIS-C.

GUIDELINES & CONSENSUS STATEMENTS

ACOG Practice Advisory: [Vaccinating Pregnant and Lactating Patients Against COVID-19](#)

[Multidisciplinary consensus on sputum induction biosafety during the COVID-19 pandemic.](#)

Allergy. 2020 Dec 12. doi: 10.1111/all.14697.

FDA / CDC / NIH / WHO Updates

CDC - [Interim Guidance on Testing Healthcare Personnel for SARS-CoV-2](#), [Interim Infection Prevention and Control Recommendations for Healthcare Personnel During the Coronavirus Disease 2019 \(COVID-19\) Pandemic](#), [Interim U.S. Guidance for Risk Assessment and Work Restrictions for Healthcare Personnel with Potential Exposure to COVID-19](#), all updated Dec 14, 2020

FDA - [Vaccines and Related Biological Products Advisory Committee Meeting December 10, 2020](#)

FDA - [Authorizes Antigen Test as First Over-the-Counter Fully At-Home Diagnostic Test for COVID-19](#)

NIH - [The COVID-19 Treatment Guidelines Panel's Statement on the Emergency Use Authorization of Baricitinib for the Treatment of COVID-19](#)

Commentary & News

[A Nursing Researcher's Experience in a COVID-19 Vaccine Trial.](#) Choi KR. *JAMA Intern Med*. December 7, 2020. doi:10.1001/jamainternmed.2020.7087 - *Commentary on importance of public messaging re: short-lasting side-effects of vaccine injection.*

[Pulmonary Fungal Infections Affect Patients with COVID-19.](#) Kuehn BM. *JAMA*. 2020 Dec 8;324(22):2248. doi: 10.1001/jama.2020.22914.

[Behaviorally Informed Strategies for a National COVID-19 Vaccine Promotion Program.](#) Volpp KG, et al. *JAMA*. December 14, 2020. doi:10.1001/jama.2020.24036

[UK probes whether COVID-19 vaccine caused allergic reactions](#)

[Health Canada authorizes first COVID-19 vaccine](#)

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