

COVID-19 Resource Desk

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New Research

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COVID-19 related publications by Providence caregivers – see [Digital Commons](#)

Basic Science / Virology / Pre-clinical

1. **Structural basis for the neutralization of SARS-CoV-2 by an antibody from a convalescent patient.** Zhou D, Duyvesteyn HME, Chen CP, et al. *Nat Struct Mol Biol.* 2020 Jul 31. doi: 10.1038/s41594-020-0480-y. <https://www.nature.com/articles/s41594-020-0480-y>
Findings: We have isolated an antibody, EY6A, from an individual convalescing from COVID-19 and have shown that it neutralizes SARS-CoV-2 and cross-reacts with SARS-CoV-1. EY6A Fab binds the receptor binding domain (RBD) of the viral spike glycoprotein tightly (KD of 2 nM), and a 2.6-Å-resolution crystal structure of an RBD-EY6A Fab complex identifies the highly conserved epitope, away from the ACE2 receptor binding site. Residues within this footprint are key to stabilizing the pre-fusion spike. Cryo-EM analyses of the pre-fusion spike incubated with EY6A Fab reveal a complex of the intact spike trimer with three Fabs bound and two further multimeric forms comprising the destabilized spike attached to Fab. EY6A binds what is probably a major neutralizing epitope, making it a candidate therapeutic for COVID-19.

Clinical Syndrome

2. **Epidemiology of invasive pulmonary aspergillosis among COVID-19 intubated patients: a prospective study.** Bartoletti M, Pascale R, Cricca M, et al. *Clin Infect Dis.* 2020 Jul 28:ciaa1065. doi: 10.1093/cid/ciaa1065. <https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa1065/5876990>
Findings: A total of 108 patients were enrolled. Probable CAPA was diagnosed in 30 (27.7%) of patients after a median of 4 days from ICU admission. Kaplan-Meier curves showed a significant higher 30-day mortality rate from ICU admission among patients with either CAPA (44% vs 19%, p= 0.002) or PIPA (74% vs 26%, p<0.001) when compared with patients not fulfilling criteria for aspergillosis. Among patients with CAPA receiving voriconazole treatment (13 patients, 43%) a trend toward lower mortality (46% vs 59% p=0.30) and reduction of galactomannan index in consecutive samples was observed. We found a high incidence of CAPA among critically ill COVID-19 patients and that its occurrence seems to change the natural history of disease.

3. **Altered mental status as a novel initial clinical presentation for COVID-19 infection in the elderly.** Ward CF et al. *Am J Geriatr Psychiatry* 2020 Aug; 28:808.
<https://www.sciencedirect.com/science/article/pii/S1064748120303420?via%3Dihub>
Findings: To date, most of the medical literature, including Center for Disease Control guidelines, has relied on three necessary symptoms in making the diagnosis of COVID-19: fever, cough, and shortness of breath. We present four cases of elderly patients who developed altered mental status as their presenting symptom without associated fever or respiratory symptoms.
4. **SARS-CoV-2-reactive T cells in healthy donors and patients with COVID-19.** Braun J, Loyal L, Frentsch M, et al. *Nature* (July 29 2020). <https://doi.org/10.1038/s41586-020-2598-9>
<https://www.nature.com/articles/s41586-020-2598-9>
Findings: Prior exposure to coronaviruses may be a factor in disease severity of COVID-19. Our study reveals pre-existing cellular SARS-CoV-2-cross-reactivity in a substantial proportion of SARS-CoV-2 seronegative HD. This finding might have significant epidemiological implications regarding herd immunity thresholds and projections for the COVID-19 pandemic. Our results provide a decisive rationale to initiate worldwide prospective studies to assess the contribution of pre-existing, potentially region-dependent SARS-CoV-2-cross-reactive immunity to the diverse clinical outcomes of SARS-CoV-2 infections.
5. **Association of Cardiac Infection with SARS-CoV-2 in Confirmed COVID-19 Autopsy Cases.** Lindner D, Fitzek A, Bräuninger H, et al. *JAMA Cardiol.* 2020 Jul 27. doi: 10.1001/jamacardio.2020.3551.
<https://jamanetwork.com/journals/jamacardiology/fullarticle/2768914>
Findings: In this analysis of autopsy cases, viral presence within the myocardium could be documented. While a response to this infection could be reported in cases with higher virus load vs no virus infection, this was not associated with an influx of inflammatory cells. Future investigations should focus on evaluating the long-term consequences of this cardiac involvement.
6. **Postmortem Kidney Pathology Findings in Patients with COVID-19.** Santoriello D, Khairallah P, Bomback AS, et al. *J Am Soc Nephrol.* 2020 Jul 29:ASN.2020050744. doi: 10.1681/ASN.2020050744.
<https://jasn.asnjournals.org/content/early/2020/07/28/ASN.2020050744>
Findings: Among patients with available data, AKI developed in 31 of 33 patients (94%), including 6 with AKI stage 1, 9 with stage 2, and 16 with stage 3. The predominant finding correlating with AKI was acute tubular injury. However, the degree of acute tubular injury was often less severe than predicted for the degree of AKI, suggesting a role for hemodynamic factors, such as aggressive fluid management. Background changes of hypertensive arterionephrosclerosis and diabetic glomerulosclerosis were frequent but typically mild. Among a cohort of 42 patients dying with COVID-19, autopsy histologic evaluation revealed acute tubular injury, which was typically mild relative to the degree of creatinine elevation. These findings suggest potential for reversibility upon resolution of SARS-CoV-2 infection.

7. **SARS-CoV-2-related atypical thyroiditis.** Muller I, Cannavaro D, Dazzi D, et al. *Lancet Diabetes Endocrinol.* 2020 Jul 30:S2213-8587(20)30266-7. doi: 10.1016/S2213-8587(20)30266-7. [https://www.thelancet.com/journals/landia/article/PIIS2213-8587\(20\)30266-7/fulltext](https://www.thelancet.com/journals/landia/article/PIIS2213-8587(20)30266-7/fulltext)

Findings: We compared patients admitted to ICUs in 2020 because of COVID-19 (HICU-20 group), with those admitted to the same ICUs in 2019, thus SARS-CoV-2 negative (HICU-19 group). Estimating a prevalence of subacute thyroiditis of 0.5% in the HICU-19 group, in line with the general population, and of 10% in the HICU-20 group. We suggest routine assessment of thyroid function in patients with COVID-19 requiring high intensity care, because they frequently present with thyrotoxicosis due to a form of subacute thyroiditis related to SARS-CoV-2. Considering the currently ongoing pandemic emergency, future studies are encouraged to confirm, or counter, these results.

8. **Incidence of co-infections and superinfections in hospitalised patients with COVID-19: a retrospective cohort study.** Garcia-Vidal C, Sanjuan G, Moreno-García E, et al. *Clin Microbiol Infect.* 2020 Jul 31:S1198-743X(20)30450-X. doi: 10.1016/j.cmi.2020.07.041.

Findings: Of a total of 989 consecutive patients with COVID-19, 72 (7.2%) had 88 other microbiologically confirmed infections: 74, bacterial; 7, fungal and 7, viral. Community-acquired co-infection at COVID-19 diagnosis was uncommon (31 out of 989, 3.1%) and mainly caused by *Streptococcus pneumoniae* and *Staphylococcus aureus*. A total of 51 hospital-acquired bacterial superinfections, mostly caused by *Pseudomonas aeruginosa* and *Escherichia coli*, were diagnosed in 43 (4.7%) patients. Overall mortality was 9.8% (97/989). Patients with community-acquired co-infections and hospital-acquired superinfections presented with worse outcomes. Co-infection at COVID-19 diagnosis is uncommon. Few patients developed superinfections during hospitalisation. Such findings could prove essential in defining the role of empiric antimicrobial therapy or stewardship strategies.

Diagnostics & Screening

9. **Prospective study comparing deep-throat saliva with other respiratory tract specimens in the diagnosis of novel coronavirus disease (COVID-19).** Lai CKC, Chen Z, Lui G, et al. *J Infect Dis.* 2020 Aug 1:jjaa487. doi: 10.1093/infdis/jjaa487.

<https://academic.oup.com/jid/article/doi/10.1093/infdis/jjaa487/5879767>

Findings: We prospectively examined 563 serial samples collected during the virus shedding periods of 50 patients: 150 deep-throat saliva (DTS), 309 pooled-nasopharyngeal (NP) and throat swabs, and 104 sputum. DTS had the lowest overall RT-PCR positive rate (68.7% vs. 89.4% [sputum] and 80.9% [pooled NP and throat swabs]), and the lowest viral RNA concentration (mean log copy/mL 3.54 vs. 5.03 [sputum] and 4.63 [pooled NP and throat swabs]). Virus yield of DTS correlated with that of sputum (Pearson correlation index [95% CI]: 0.76 [0.62 - 0.86]). We estimated the overall false-negative rate of DTS could be 31.3%, and increased 2.7 times among patients without sputum. DTS produced the lowest viral RNA concentration and RT-PCR positive rate compared to conventional respiratory specimens in all phases of illness. Self-collect sputum should be the choice for patients with sputum.

10. **Validation of small-size-pooling approach targeted to hospital surveillance of SARS-CoV-2 infection.** Petrucca A, Borro M, Lionetto L, et al. *Infect Control Hosp Epidemiol.* 2020 Jul 30:1-6. doi: 10.1017/ice.2020.380. <https://tinyurl.com/y2yhkzk2>

Findings: When SARS-CoV-2 infection incidence is low, as in our study (below 2%), the small-pooling approach significantly reduces the use of laboratory resources and simultaneously increases the number of screened people. The number of positive pools to be re-analysed increases in relation to SARS-CoV-2 incidence, consequently worsening TAT and cost-benefit ratio. This approach represents an optimal strategy for surveillance programs in late pandemic phases, when screening of large population is needed.

Epidemiology & Public Health

11. **Association between Statewide School Closure and COVID-19 Incidence and Mortality in the US.** Auger KA, Shah SS, Richardson T, et al. *JAMA.* July 29, 2020. doi:10.1001/jama.2020.14348 <https://jamanetwork.com/journals/jama/fullarticle/2769034>

Findings: In this US population-based time series analysis conducted between March 9, 2020, and May 7, 2020, school closure was associated with a significant decline in both incidence of COVID-19 (adjusted relative change per week, -62%) and mortality (adjusted relative change per week, -58%). In a model derived from this analysis, it was estimated that closing schools when the cumulative incidence of COVID-19 was in the lowest quartile compared with the highest quartile was associated with 128.7 fewer cases per 100,000 population over 26 days and with 1.5 fewer deaths per 100,000 population over 16 days. There was a temporal association between statewide school closure and lower COVID-19 incidence and mortality, although some of the reductions may have been related to other concurrent non-pharmaceutical interventions.

12. **A prospective cohort study in non-hospitalized household contacts with SARS-CoV-2 infection: symptom profiles and symptom change over time.** Yousaf AR, Duca LM, Chu V, et al. *Clin Infect Dis.* 2020 Jul 28:ciaa1072. doi: 10.1093/cid/ciaa1072. <https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa1072/5877084>

Findings: We identified 47 contacts, median age 24 (3-75) years, with detectable SARS-CoV-2 by RT-PCR. The most commonly reported symptoms on the day of first positive RT-PCR test were upper respiratory (68%) and neurologic (64%); fever was not commonly reported (19%). Eight (17%) individuals were asymptomatic at the date of first positive RT-PCR collection; two (4%) had preceding symptoms that resolved and six (13%) subsequently developed symptoms. Children less frequently reported lower respiratory symptoms (age <18: 21%, age 18-49: 60%, age 50+ years: 69%; p=0.03). CONCLUSIONS: Household contacts with lab-confirmed SARS-CoV-2 infection reported mild symptoms. When assessed at a single time-point, several contacts appeared to have asymptomatic infection; however, over time all developed symptoms. These findings are important to inform infection control, contact tracing, and community mitigation strategies.

13. **Comparison of Weighted and Unweighted Population Data to Assess Inequities in Coronavirus Disease 2019 Deaths by Race/Ethnicity Reported by the US Centers for Disease**

Control and Prevention. Cowger TL, Davis BA, Etkins OS, et al. *JAMA Netw Open.* 2020 Jul 1;3(7):e2016933. doi: 10.1001/jamanetworkopen.2020.16933.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2768722>

Findings: Use of the CDC's weighted population distributions to evaluate racial/ethnic inequities in COVID-19 mortality underestimates the excess burden of COVID-19 among Black and Latinx individuals compared with analyses conducted using the total population (unweighted) in the US Census data. In summary, the CDC's presentation of data on race/ethnicity and COVID-19 deaths is misleading, with consequences for resource allocation for mitigating health inequities. We urge the CDC to drop the misleading weighted counts and publish mortality rates per race/ethnicity group stratified by age, gender, education, and ZIP code characteristics to adequately equip epidemiologists and policy makers with the data to mitigate inequities.

14. **Age-Related Differences in Nasopharyngeal Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Levels in Patients with Mild to Moderate Coronavirus Disease 2019 (COVID-19).** Heald-Sargent T, Muller WJ, Zheng X, et al. *JAMA Pediatr.* July 30, 2020.

doi:10.1001/jamapediatrics.2020.3651

<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2768952>

Findings: Our analyses suggest children younger than 5 years with mild to moderate COVID-19 have high amounts of SARS-CoV-2 viral RNA in their nasopharynx compared with older children and adults. Our study is limited to detection of viral nucleic acid, rather than infectious virus, although SARS-CoV-2 pediatric studies reported a correlation between higher nucleic acid levels and the ability to culture infectious virus. Thus, young children can potentially be important drivers of SARS-CoV-2 spread in the general population, as has been demonstrated with respiratory syncytial virus, where children with high viral loads are more likely to transmit. Behavioral habits of young children and close quarters in school and day care settings raise concern for SARS-CoV-2 amplification in this population as public health restrictions are eased. In addition to public health implications, this population will be important for targeting immunization efforts as SARS-CoV-2 vaccines become available.

15. **Assessing racial and ethnic disparities using a COVID-19 outcomes continuum for New York State.** Holtgrave DR, Barranco MA, Tesoriero JM, et al. *Ann Epidemiol.* 2020 Jun 29;48:9-14. doi: 10.1016/j.annepidem.2020.06.010.

<https://www.sciencedirect.com/science/article/pii/S1047279720302076>

Findings: Estimated per-population COVID-19 fatality rates were 0.03%, 0.18%, and 0.12% for white non-Hispanic, Black non-Hispanic, and Hispanic adults, respectively. The 3.48-fold disparity for Hispanic, relative to white, communities was explained by differences in infection experience, whereas the 5.38-fold disparity for non-Hispanic Black, relative to white, communities was primarily driven by differences in both infection experience and in the need for hospitalization, given infection. These findings suggest the most impactful stages on which to intervene with programs and policies to build COVID-19 health equity.

16. **Symptom Duration and Risk Factors for Delayed Return to Usual Health among Outpatients with COVID-19 in a Multistate Health Care Systems Network - United States, March-June 2020.** Tenforde MW, Kim SS, Lindsell CJ, et al. *MMWR Morb Mortal Wkly Rep.* 2020 Jul

31;69(30):993-998. doi: 10.15585/mmwr.mm6930e1.

<https://www.cdc.gov/mmwr/volumes/69/wr/mm6930e1.htm>

Findings: Among 292 respondents, 94% (274) reported experiencing one or more symptoms at the time of testing; 35% of these symptomatic respondents reported not having returned to their usual state of health by the date of the interview (median = 16 days from testing date), including 26% among those aged 18-34 years, 32% among those aged 35-49 years, and 47% among those aged ≥50 years. Among respondents reporting cough, fatigue, or shortness of breath at the time of testing, 43%, 35%, and 29%, respectively, continued to experience these symptoms at the time of the interview. These findings indicate that COVID-19 can result in prolonged illness even among persons with milder outpatient illness, including young adults.

17. **A model of disparities: risk factors associated with COVID-19 infection.** Yelena Rozenfeld, Jennifer Beam, Haley Maier, Whitney Haggerson, Karen Boudreau, Jamie Carlson, Rhonda Medows [PSJH authors]. *Int J Equity Health*. 2020 Jul 29;19(1):126. doi: 10.1186/s12939-020-01242-z.

<https://equityhealthj.biomedcentral.com/track/pdf/10.1186/s12939-020-01242-z>

Findings: A multivariable statistical model was used to characterize risk factors in 34,503 cases of laboratory-confirmed positive or negative COVID-19 infection in the Providence Health System (U.S.) between February 28 and April 27, 2020. Higher risk of COVID-19 infection was associated with older age, male gender, Asian race, Black/African American race, Latino ethnicity, non-English language, residing in a neighborhood with financial insecurity, low air quality, housing insecurity or transportation insecurity, and living in senior living communities. Risk of COVID-19 infection is higher among groups already affected by health disparities across age, race, ethnicity, language, income, and living conditions. Health promotion and disease prevention strategies should prioritize groups most vulnerable to infection and address structural inequities that contribute to risk through social and economic policy.

18. **Risk of COVID-19 among front-line health-care workers and the general community: a prospective cohort study.** Nguyen LH, Drew DA, Graham MS, et al. *Lancet Public Health*. 2020 Jul 30:S2468-2667(20)30164-X. doi: 10.1016/S2468-2667(20)30164-X.

[https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667\(20\)30164-X/fulltext](https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(20)30164-X/fulltext)

Findings: Among 2,035,395 community individuals and 99,795 front-line health-care workers, we recorded 5,545 incident reports of a positive COVID-19 test over 34,435,272 person-days. Compared with the general community, front-line health-care workers were at increased risk for reporting a positive COVID-19 test (adjusted HR 11.61). To account for differences in testing frequency between front-line health-care workers and the general community and possible selection bias, an inverse probability-weighted model was used to adjust for the likelihood of receiving a COVID-19 test (adjusted HR 3.40). Secondary and post-hoc analyses suggested adequacy of PPE, clinical setting, and ethnic background were also important factors. In the UK and the USA, risk of reporting a positive test for COVID-19 was increased among front-line health-care workers. Health-care systems should ensure adequate availability of PPE and develop additional strategies to protect health-care workers from COVID-19, particularly those from Black, Asian, and minority ethnic backgrounds.

Healthcare Delivery & Healthcare Workers

19. **Income Disparities in Access to Critical Care Services.** Kanter GP, Segal AG, Groeneveld PW. *Health Aff (Millwood)*. 2020 Aug;39(8):1362-1367. doi: 10.1377/hlthaff.2020.00581. <https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.2020.00581>
Findings: We examined disparities in community ICU beds by US communities' median household income. We found a large gap in access by income: 49 percent of the lowest-income communities had no ICU beds in their communities, whereas only 3 percent of the highest-income communities had no ICU beds. Income disparities in the availability of community ICU beds were more acute in rural areas than in urban areas. Policies that facilitate hospital coordination are urgently needed to address shortages in ICU hospital bed supply to mitigate the effects of the COVID-19 pandemic on mortality rates in low-income communities.
20. **Trends in Emergency Department Visits and Hospital Admissions in Health Care Systems in 5 States in the First Months of the COVID-19 Pandemic in the US.** Jeffery MM, D'Onofrio G, Paek H, et al. *JAMA Intern Med*. August 3, 2020. doi:10.1001/jamainternmed.2020.3288 <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2768777?resultClick=1>
Findings: In this cross-sectional study of 24 emergency departments in 5 health care systems in Colorado, Connecticut, Massachusetts, New York, and North Carolina, decreases in emergency department visits ranged from 41.5% in Colorado to 63.5% in New York, with the most rapid rates of decrease in visits occurring in early March 2020. Rates of hospital admissions from the ED were stable until new COVID-19 case rates began to increase locally, at which point relative increases in hospital admission rates ranged from 22.0% to 149.0%.

Laboratory Results

24. **Differences in antibody kinetics and functionality between severe and mild SARS-CoV-2 infections.** Rijkers G, Murk JL, Wintermans B, et al. *J Infect Dis*. 2020 Jul 29;jiaa463. doi: 10.1093/infdis/jiaa463. <https://academic.oup.com/jid/article/doi/10.1093/infdis/jiaa463/5877927>
Findings: We determined and compared the humoral immune response in severe, hospitalized and mild, non-hospitalized COVID-19 patients. Severe patients (n=38) develop a robust antibody response to SARS-CoV-2, including IgG and IgA antibodies. The geometric mean 50% virus neutralization titer is 1:240. SARS-CoV-2 infected hospital personnel (n=24), who developed mild symptoms necessitating leave of absence, self-isolation, but not hospitalization, 75 % develop antibodies, but with low/absent virus neutralization (60% < 1:20). While severe COVID-19 patients develop a strong antibody response, mild SARS-CoV-2 infections induce a modest antibody response. Long term monitoring will show whether these responses predict protection against future infections.
25. **Abnormal Liver Tests in COVID-19: A Retrospective Observational Cohort Study of 1827 Patients in a Major U.S. Hospital Network.** Hundt MA, Deng Y, Ciarleglio MM, et al. *Hepatology*. 2020 Jul 29. doi: 10.1002/hep.31487. <https://aasldpubs.onlinelibrary.wiley.com/doi/10.1002/hep.31487>

Findings: We conducted a retrospective cohort study of 1827 patients with confirmed COVID-19 who were hospitalized within the Yale-New Haven Health System between March 14, 2020 and April 23, 2020. Clinical characteristics, liver tests (AST, ALT, ALP, TBIL, albumin) at three time points (pre-infection baseline, admission, peak hospitalization), and hospitalization outcomes (severe COVID-19, ICU admission, mechanical ventilation, death) were analyzed. Abnormal liver tests were commonly observed in hospitalized patients with COVID-19, both at admission (AST 66.9%, ALT 41.6%, ALP 13.5%, TBIL 4.3%) and peak hospitalization (AST 83.4%, ALT 61.6%, ALP 22.7%, TBIL 16.1%). Most patients with abnormal liver tests at admission had minimal elevations 1-2x ULN (AST 63.7%, ALT 63.5%, ALP 80.0%, TBIL 75.7%). A significant proportion of these patients had abnormal liver tests pre-hospitalization (AST 25.9%, ALT 38.0%, ALP 56.8%, TBIL 44.4%). Multivariate analysis revealed an association between abnormal liver tests and severe COVID-19, including ICU admission, mechanical ventilation, and death; associations with age, male gender, BMI, and diabetes mellitus were also observed. Medications used in COVID-19 treatment (lopinavir/ritonavir, hydroxychloroquine, remdesivir, and tocilizumab) were associated with peak hospitalization liver transaminase elevations >5x ULN. Conclusion: Abnormal liver tests occur in most hospitalized patients with COVID-19 and may be associated with poorer clinical outcomes.

Prognosis

26. **Body Mass Index and Risk for Intubation or Death in SARS-CoV-2 Infection: A Retrospective Cohort Study.** Anderson MR, Geleris J, Anderson DR, et al. *Ann Intern Med.* 2020 Jul 29. doi: 10.7326/M20-3214. <https://www.acpjournals.org/doi/10.7326/M20-3214>
Findings: Over a median hospital length of stay of 7 days (interquartile range, 3 to 14) days, 533 patients (22%) were intubated, 627 (25%) died, and 59 (2%) remained hospitalized. Compared with overweight patients, patients with obesity had higher risk for intubation or death, with the highest risk among those with class 3 obesity. This association was primarily observed among patients younger than 65 years and not in older patients. Body mass index was not associated with admission levels of biomarkers of inflammation, cardiac injury, or fibrinolysis. Obesity is associated with increased risk for intubation or death from COVID-19 in adults younger than 65 years, but not in adults aged 65 years or older.
27. **Prognostic value of serum amyloid A in patients with COVID-19.** Cheng L, Yang JZ, Bai WH, et al. *Infection.* 2020 Jul 30. doi: 10.1007/s15010-020-014687. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7391472/>
Findings: This study is based on the clinical outcomes of COVID-19 patients after admission, affirming the value of SAA in the prognosis judgment of patients with COVID-19. Dynamically monitoring the changes in SAA to adopt an effective diagnosis and treatment strategy for COVID-19 patients in the early stage may improve the survival rate of patients.
28. **Prediction model and risk scores of ICU admission and mortality in COVID-19.** Zhao Z, Chen A, Hou W, et al. *PLoS One.* 2020 Jul 30;15(7):e0236618. doi: 10.1371/journal.pone.0236618. eCollection 2020. <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0236618>

Findings: Five significant variables predicting ICU admission were lactate dehydrogenase, procalcitonin, pulse oxygen saturation, smoking history, and lymphocyte count. Seven significant variables predicting mortality were heart failure, procalcitonin, lactate dehydrogenase, chronic obstructive pulmonary disease, pulse oxygen saturation, heart rate, and age. The mortality group uniquely contained cardiopulmonary variables. The risk score model yielded good accuracy with an AUC of 0.74 ([95% CI, 0.63-0.85], $p = 0.001$) for predicting ICU admission and 0.83 ([95% CI, 0.73-0.92], $p < 0.001$) for predicting mortality for the testing dataset. This study identified key independent clinical variables that predicted ICU admission and mortality associated with COVID-19. This risk score system may prove useful for frontline physicians in clinical decision-making under time-sensitive and resource-constrained environment.

29. **Comparative study of lung ultrasound and chest computed tomography scan in the assessment of severity of confirmed COVID-19 pneumonia.** Zieleskiewicz L, Markarian T, Lopez A, et al. *Intensive Care Med.* 2020 Jul 29. doi: 10.1007/s00134-020-06186-0.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7388119/>

Findings: In known SARS-CoV-2 pneumonia patients, the LUS score was predictive of pneumonia severity as assessed by a chest CT scan and clinical features. Within the limitations inherent to our study design, LUS can be used to assess SARS-CoV-2 pneumonia severity.

30. **Risk of severe COVID-19 disease with ACE inhibitors and angiotensin receptor blockers: cohort study including 8.3 million people.** Hippisley-Cox J, Young D, Coupland C, et al. *Heart.* 2020 Jul 31;heartjnl-2020-317393. doi: 10.1136/heartjnl-2020-317393.

<https://heart.bmj.com/content/early/2020/07/31/heartjnl-2020-317393>

Findings: ACE inhibitors and ARBs are associated with reduced risks of COVID-19 disease after adjusting for a wide range of variables. Neither ACE inhibitors nor ARBs are associated with significantly increased risks of receiving ICU care. Variations between different ethnic groups raise the possibility of ethnic-specific effects of ACE inhibitors/ARBs on COVID-19 disease susceptibility and severity which deserves further study.

31. **Development of a work of breathing scale and monitoring need of intubation in COVID-19 pneumonia.** Apigo M, Schechtman J, Dhliwayo N, et al. *Crit Care.* 2020 Jul 31;24(1):477. doi: 10.1186/s13054-020-03176-y. <https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-03176-y>

Findings: We tested the ability of healthcare providers to rapidly learn and apply our WOB scale. We first trained a team of “super-raters” composed of ICU nurses and internal medicine residents. Next, we identified a group of nurses, medical students, residents, and attendings naïve to the WOB scale and designated them as “raters”. Super-raters trained raters using a 4-min WOB scale video and tested their ability to correctly rate the WOB level in 80 non-intubated patients from the Emergency Department, medical wards, and the ICU with WOB ranging from 1 to 5. A total of three assessments per patient were completed showing a high correlation between the super-raters and raters 1 ($r = 0.93$; $p < 0.001$), super-raters and raters 2 ($r = 0.91$; $p < 0.001$), and between the two raters ($r = 0.84$; $p < 0.001$). In addition, the interrater

reliability between the two raters measured by the Krippendorf's α test was also high at 0.85 (95% CI, 0.78–0.91).

32. **Mortality in COVID-19 patients with acute respiratory distress syndrome and corticosteroids use: a systematic review and meta-analysis.** Hasan SS, Capstick T, Ahmed R, et al. *Expert Rev Respir Med.* 2020 Jul 31. doi: 10.1080/17476348.2020.1804365. <https://www.tandfonline.com/doi/full/10.1080/17476348.2020.1804365>
Findings: The high mortality in COVID-19 associated ARDS necessitates a prompt and aggressive treatment strategy including corticosteroids. Most of the studies included no information on the dosing regimen of corticosteroid therapy, however, low-dose corticosteroid therapy or pulse corticosteroid therapy appears to have a beneficial role in the management of severely ill COVID-19 patients.

Survivorship & Rehabilitation

33. **Pulmonary function in patients surviving to COVID-19 pneumonia.** Fumagalli A, Misuraca C, Bianchi A, et al. *Infection.* 2020 Jul 28. doi: 10.1007/s15010-020-01474-9. <https://link.springer.com/article/10.1007/s15010-020-01474-9>
Findings: Our findings suggest that COVID-19 pneumonia may result in clinically relevant alterations in pulmonary function tests, with a mainly restrictive pattern.
34. **Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19).** Puntmann VO, Carerj ML, Wieters I, et al. *JAMA Cardiol.* 2020 Jul 27. doi: 10.1001/jamacardio.2020.3557. <https://jamanetwork.com/journals/jamacardiology/fullarticle/2768916>
Findings: In this study of a cohort of German patients recently recovered from COVID-19 infection, CMR revealed cardiac involvement in 78 patients (78%) and ongoing myocardial inflammation in 60 patients (60%), independent of preexisting conditions, severity and overall course of the acute illness, and time from the original diagnosis. These findings indicate the need for ongoing investigation of the long-term cardiovascular consequences of COVID-19.
35. **Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation.** Halpin SJ, McIvor C, Whyatt G, et al. *J Med Virol.* 2020 Jul 30. doi: 10.1002/jmv.26368. <https://onlinelibrary.wiley.com/doi/10.1002/jmv.26368>
Findings: Participants were between 29 and 71 days post-discharge from hospital. Thirty-two participants required treatment in intensive care and 68 were managed in hospital wards without needing ICU care. New illness-related fatigue was the most common reported symptom by 72% participants in ICU group and 60.3% in ward group. The next most common symptoms were breathlessness (65.6% in ICU group; 42.6% in ward group) and psychological distress (46.9% in ICU group; 23.5% in ward group). We recommend planning rehabilitation services to manage these symptoms appropriately and maximise the functional return of COVID-19 survivors.

Therapeutics

36. **Drug treatments for covid-19: living systematic review and network meta-analysis.** Siemieniuk RA, Bartoszko JJ, Ge L, et al. *BMJ*. 2020 Jul 30;370:m2980. doi: 10.1136/bmj.m2980. <https://www.bmj.com/content/370/bmj.m2980>
Findings: 23 randomised controlled trials were included in the analysis performed on 26 June 2020. The certainty of the evidence for most comparisons was very low because of risk of bias (lack of blinding) and serious imprecision. Glucocorticoids were the only intervention with evidence for a reduction in death compared with standard care (risk difference 37 fewer per 1000 patients, 95% credible interval 63 fewer to 11 fewer, moderate certainty) and mechanical ventilation (31 fewer per 1000 patients, 47 fewer to 9 fewer, moderate certainty). These estimates are based on direct evidence; network estimates for glucocorticoids compared with standard care were less precise because of network heterogeneity. Three drugs might reduce symptom duration compared with standard care: hydroxychloroquine (mean difference -4.5 days, low certainty), remdesivir (-2.6 days, moderate certainty), and lopinavir-ritonavir (-1.2 days, low certainty). Hydroxychloroquine might increase the risk of adverse events compared with the other interventions, and remdesivir probably does not substantially increase the risk of adverse effects leading to drug discontinuation. No other interventions included enough patients to meaningfully interpret adverse effects leading to drug discontinuation. Glucocorticoids probably reduce mortality and mechanical ventilation in patients with covid-19 compared with standard care. The effectiveness of most interventions is uncertain because most of the randomised controlled trials so far have been small and have important study limitations.
37. **Historically controlled comparison of glucocorticoids with or without tocilizumab versus supportive care only in patients with COVID-19-associated cytokine storm syndrome: results of the CHIC study.** Ramiro S, Mostard RLM, Magro-Checa C, et al. *Ann Rheum Dis*. 2020 Jul 20;annrheumdis-2020-218479. doi: 10.1136/annrheumdis-2020-218479. <https://ard.bmj.com/content/early/2020/07/20/annrheumdis-2020-218479>
Findings: At baseline all patients with COVID-19 in the treatment group (n=86) and control group (n=86) had symptoms of CSS and faced acute respiratory failure. Treated patients had 79% higher likelihood on reaching the primary outcome (HR: 1.8; 95% CI 1.2 to 2.7) (7 days earlier), 65% less mortality (HR: 0.35; 95% CI 0.19 to 0.65) and 71% less invasive mechanical ventilation (HR: 0.29; 95% CI 0.14 to 0.65). Treatment effects remained constant in confounding and sensitivity analyses. A strategy involving a course of high-dose methylprednisolone, followed by tocilizumab if needed, may accelerate respiratory recovery, lower hospital mortality and reduce the likelihood of invasive mechanical ventilation in COVID-19-associated CSS.
38. **Pharmacokinetics/Pharmacodynamics of Antiviral Agents Used to Treat SARS-CoV-2 and Their Potential Interaction with Drugs and Other Supportive Measures: A Comprehensive Review by the PK/PD of Anti-Infectives Study Group of the European Society of Antimicrobial Agents.** Zeitlinger M, Koch BCP, Bruggemann R, et al. *Clin Pharmacokinet*. 2020 Jul 28. doi: 10.1007/s40262-020-00924-9. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7385074/>

Findings: We have conducted a rapid and comprehensive review of relevant pharmacological evidence, focusing on (1) the pharmacokinetics (PK) of potential antiviral therapies; (2) coronavirus-specific pharmacodynamics (PD); (3) PK and PD interactions between proposed combination therapies; (4) pharmacology of major supportive therapies; and (5) anticipated drug-drug interactions (DDIs). We found promising in vitro evidence for remdesivir, (hydroxy)chloroquine and favipiravir against SARS-CoV-2; potential clinical benefit in SARS-CoV-2 with remdesivir, the combination of lopinavir/ritonavir (LPV/r) plus ribavirin; and strong evidence for LPV/r plus ribavirin against Middle East Respiratory Syndrome (MERS) for post-exposure prophylaxis in healthcare workers. Despite these emerging data, robust controlled clinical trials assessing patient-centred outcomes remain imperative and clinical data have already reduced expectations with regard to some drugs. Any therapy should be used with caution in the light of potential drug interactions and the uncertainty of optimal doses for treating mild versus serious infections.

39. **Early administration of Interleukin-6 inhibitors for patients with severe Covid-19 disease is associated with decreased intubation, reduced mortality, and increased discharge.** Sinha P, Mostaghim A, Bielick CG, et al. *Int J Infect Dis.* 2020 Jul 25:S1201-9712(20)30568-3. doi: 10.1016/j.ijid.2020.07.023. [https://www.ijidonline.com/article/S1201-9712\(20\)30568-3/fulltext](https://www.ijidonline.com/article/S1201-9712(20)30568-3/fulltext)
Findings: 255 Covid-19 patients were treated with IL6ri (149 stage IIB and 106 stage III). Patients treated in stage IIB had lower mortality than the stage III group (adjusted hazard ratio [aHR]: 0.24; 95% confidence interval [CI] 0.08-0.74). Overall, 218 (85.5%) patients were discharged alive. Patients treated in stage IIB were more likely to be discharged (aHR: 1.43; 95% CI 1.06 - 1.93) and were less likely to be intubated (HR: 0.43; 95% CI: 0.24-0.79). IL6ri administration prior to greater than 45% FiO2 requirement was associated with improved Covid-19 outcomes. This can guide clinical management pending results from randomized control trials.
40. **Association between treatment with colchicine and improved survival in a single-centre cohort of adult hospitalised patients with COVID-19 pneumonia and acute respiratory distress syndrome.** Scarsi M, Piantoni S, Colombo E, et al. *Ann Rheum Dis.* 2020 Jul 30:annrheumdis-2020-217712. doi: 10.1136/annrheumdis-2020-217712. <https://ard.bmj.com/content/early/2020/07/30/annrheumdis-2020-217712>
Findings: Patients treated with colchicine had a better survival rate as compared with SoC at 21 days of follow-up (84.2% (SE=3.3%) vs 63.6% (SE=4.1%), p=0.001). Cox proportional hazards regression survival analysis showed that a lower risk of death was independently associated with colchicine treatment (HR=0.151 (95% CI 0.062 to 0.368), p<0.0001), whereas older age, worse PaO2/FiO2, and higher serum levels of ferritin at entry were associated with a higher risk. This proof-of-concept study may support the rationale of use of colchicine for the treatment of COVID-19. Efficacy and safety must be determined in controlled clinical trials.
41. **Antirheumatic Disease Therapies for the Treatment of COVID-19: A Systematic Review and Meta-analysis.** Putman M, Chock YPE, Tam H, et al. *Arthritis Rheumatol.* 2020 Aug 2. doi: 10.1002/art.41469. <https://onlinelibrary.wiley.com/doi/10.1002/art.41469>
Findings: The search identified 3,935 articles, of which 45 were included (4 randomized controlled trials, 29 cohort studies, and 12 case series). All studies evaluated hospitalized

patients and 29 out of 45 had been published in a peer-reviewed journal. In this systematic review and meta-analysis, hydroxychloroquine use was not associated with benefit or harm with regard to COVID-19 mortality. The evidence supporting the effect of other antirheumatic disease therapies in COVID-19 is currently inconclusive.

42. **Venous thromboembolism in critically ill COVID-19 patients receiving prophylactic or therapeutic anticoagulation: a systematic review and meta-analysis.** Hasan SS, Radford S, Kow CS, Zaidi STR. *J Thromb Thrombolysis*. 2020 Aug 3. doi: 10.1007/s11239-020-02235-z.

<https://link.springer.com/article/10.1007/s11239-020-02235-z>

Findings: We included twelve studies (8 Europe; 2 UK; 1 each from the US and China) in our systematic review and meta-analysis. All studies utilized LMWH or unfractionated heparin as their pharmacologic thromboprophylaxis, either prophylactic doses or therapeutic doses. Seven studies reported on the proportion of patients with the previous history of VTE (range 0-10%). The pooled prevalence of VTE among ICU patients receiving prophylactic or therapeutic anticoagulation across all studies was 31% (95% CI 20-43%). Subgroup pooled analysis limited to studies reported prophylactic anticoagulation alone and mixed (therapeutic and prophylactic anticoagulation) reported pooled prevalences of VTE of 38% (95% CI 10-70%) and 27% (95% CI 17-40%) respectively. With a high prevalence of thromboprophylaxis failure among COVID-19 patients admitted to intensive care units, individualised rather than protocolised VTE thromboprophylaxis would appear prudent at interim.

43. **Use of the IL-6R Antagonist Tocilizumab in Hospitalized COVID-19 Patients.** Patel K, Gooley TA, Bailey N, Bailey M, Hegerova L, Batchelder A, Holdread H, Dunleavy V, Downey T, Frisvold J, Megrath S, Pagarigan K, Szeto J, Rueda J, Islam A, Maree C, Nyatsatsang S, Bork SE, Lipke A, O'Mahony DS, Wagner T, Pulido J, Mignone J, Youssef S, Hartman M, Goldman JD, Pagel JM. [PSJH Authors]. *J Intern Med*. 2020 Aug 3. doi: 10.1111/joim.13163.

<https://onlinelibrary.wiley.com/doi/epdf/10.1111/joim.13163>

Findings: In this retrospective cohort study, we report on use of tocilizumab in the treatment of severely and critically ill hospitalized COVID-19 patients. Notably, in severe illness patients treated with tocilizumab, the rate of death by day 7 was less than in matched controls (14.2% vs 28.6%) with also slightly higher rate of discharge (33.3% vs 28.6%) in tocilizumab-treated patients, suggesting benefit of tocilizumab in the subgroup of severe illness patients. Mortality was similar overall in all tocilizumab-treated patients and control patients. The overall mortality of our tocilizumab-treated patients was low in comparison to historical cohorts of hospitalized patients. For patients with severe illness, defined primarily by impairment in oxygenation, approximately 15-20% of historical patients required transfer to the ICU and/or MV. In our series, only 9.5% of severely ill patients treated with tocilizumab required MV, with one patient since discharged from the hospital. Our patients receiving tocilizumab may have lower rates of ICU transfer or initiation of MV than those who do not receive anti-cytokine therapy.

Transmission / Infection Control

44. **Efficacy and safety of decontamination for N95 respirator reuse: a systematic literature search and narrative synthesis.** Steinberg BE, Aoyama K, McVey M, et al. *Can J Anaesth.* 2020 Jul 27. doi: 10.1007/s12630-020-01770-w.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7384726/>
Findings: Our initial database search resulted in five articles that met inclusion criteria, with 26 articles added from the expanded search. Our search did not reveal any relevant randomized clinical trials or cohort studies. We found that moist mask heating (65-80°C at 50-85% relative humidity for 20-30 min) and vaporous hydrogen peroxide treatment were supported by the literature to provide consistent viral decontamination without compromising mask seal and filtration efficiency. Other investigated decontamination methods lacked comprehensive scientific evidence for all three of these key criteria. N95 mask reprocessing using either moist heat or vaporous hydrogen peroxide is recommended to ensure healthcare worker safety.
45. **Virucidal efficacy of different oral rinses against SARS-CoV-2.** Meister TL, Brüggemann Y, Todt D, et al. *J Infect Dis.* 2020 Jul 29:jiaa471. doi: 10.1093/infdis/jiaa471.
<https://academic.oup.com/jid/article/doi/10.1093/infdis/jiaa471/5878067>
Findings: Here, we evaluated the virucidal activity of different available oral rinses against SARS-CoV-2 under conditions mimicking nasopharyngeal secretions. Several formulations with significant SARS-CoV-2 inactivating properties in vitro support the idea that oral rinsing might reduce the viral load of saliva and could thus lower the transmission of SARS-CoV-2.
46. **Effect of moist heat reprocessing of N95 respirators on SARS-CoV-2 inactivation and respirator function.** Daeschler SC, Manson N, Joachim K, et al. *CMAJ.* 2020 Jul 30:cmaj.201203. doi: 10.1503/cmaj.201203. <https://www.cmaj.ca/content/early/2020/07/30/cmaj.201203>
Findings: A single heat treatment rendered SARS-CoV-2 undetectable in all mask samples. Compared with untreated inoculated control masks, E. coli cultures at 24 hours were virtually undetectable from masks treated at 70°C and 50% relative humidity (optical density at 600 nm wavelength, 0.02 ± 0.02 v. 2.77 ± 0.09 , $p < 0.001$), but contamination persisted for masks treated at lower relative humidity. After 10 disinfection cycles, masks maintained fibre diameters similar to untreated masks and continued to meet standards for fit, filtration efficiency and breathing resistance. Thermal disinfection successfully decontaminated N95 respirators without impairing structural integrity or function. This process could be used in hospitals and long-term care facilities with commonly available equipment to mitigate the depletion of N95 masks.
47. **Decontamination and reuse of surgical masks and N95 filtering facepiece respirators during COVID-19 pandemic: a systematic review.** Seresirikachorn K, Phoophiboon V, Chobarporn T, et al. *Infect Control Hosp Epidemiol.* 2020 Jul 30:1-39. doi: 10.1017/ice.2020.379.
<https://tinyurl.com/y62eqbun>
Findings: Fifteen studies and fourteen decontamination methods were identified. Low level of evidence supported four decontamination methods, which were ultraviolet germicidal irradiation (9 studies), moist heat (5 studies), microwave generated steam (4 studies), and

hydrogen peroxide vapor (4 studies). Therefore, recommendations as an 'option' were given to these four methods while 'recommendation against' was given to the other ten methods.

CONCLUSIONS: Low level of evidence supported the use of ultraviolet germicidal irradiation, moist heat, microwave generated steam, and hydrogen peroxide vapor for decontamination and reuse of N95 FFRs. These decontamination methods were effective for virus and bacterial disinfection, and restoration of the filtration efficiency and the physical structure of the FFRs.

48. **Masks Do More Than Protect Others During COVID-19: Reducing the Inoculum of SARS-CoV-2 to Protect the Wearer.** Gandhi M, Beyrer C, Goosby E. *J Gen Intern Med.* 2020 Jul 31:1-4. doi: 10.1007/s11606-020-06067-8. <https://link.springer.com/article/10.1007/s11606-020-06067-8>

Findings: Although the benefit of population-level public facial masking to protect others during the COVID-19 pandemic has received a great deal of attention, we discuss for one of the first times the hypothesis that universal masking reduces the "inoculum" or dose of the virus for the mask-wearer, leading to more mild and asymptomatic infection manifestations. Masks, depending on type, filter out the majority of viral particles, but not all. We first discuss the near-century-old literature around the viral inoculum and severity of disease (conceptualized as the LD50 or lethal dose of the virus). We include examples of rising rates of asymptomatic infection with population-level masking, including in closed settings (e.g., cruise ships) with and without universal masking. Asymptomatic infections may be harmful for spread but could actually be beneficial if they lead to higher rates of exposure. Exposing society to SARS-CoV-2 without the unacceptable consequences of severe illness with public masking could lead to greater community-level immunity and slower spread as we await a vaccine. This theory of viral inoculum and mild or asymptomatic disease with SARS-CoV-2 in light of population-level masking has received little attention so this is one of the first perspectives to discuss the evidence supporting this theory.

49. **Stockpiled N95 respirator/surgical mask release beyond manufacturer-designated shelf-life: a French experience.** Brun D, Curti C, Mekideche T, et al. *J Hosp Infect.* 2020 Jul 31:S0195-6701(20)30363-7. doi: 10.1016/j.jhin.2020.07.032.

Findings: To reduce the shortage of N95 respirators and surgical masks during the COVID-19 pandemic, stockpiled equipment beyond its expiry date could be released. Tests of compliance with health authority directives were developed and carried out on 175 batches of N95 masks and 31 batches of surgical masks from 12th March 2020 to 16 April 2020. Forty-nine per cent of FFP2 mask batches were compliant with directives, 32% of batches were compliant but with some concerns and 19% of batches were non-compliant. For surgical masks, 58% of batches were compliant, 39% of batches compliant but with concerns and 3% of batches were non-compliant. The main areas of non-compliance were the breaking strength of the elastic ties and the nose clip but these alone were not considered to make the masks unacceptable. Only mask appearance and face-fit results were decisive non-compliance criteria.

50. **Characteristics and transmission dynamics of COVID-19 in healthcare workers at a London teaching hospital.** Zheng C, Hafezi-Bakhtiari N, Cooper V, et al. *J Hosp Infect.* 2020 Jul 27:S0195-6701(20)30356-X. doi: 10.1016/j.jhin.2020.07.025.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7384992/>

Findings: COVID-19 rates in our HCWs largely rose and declined in parallel with the number of community cases. White and non-white ethnic groups among our HCWs had similar rates of infection. Clinical staff had a higher rate of laboratory-confirmed COVID-19 than non-clinical staff, but total sickness rates were similar. Doctors had the highest rate of infection, but took the fewest sickness days. Critical Care had lower rates than the Emergency Department (ED), but rates in the ED declined once all staff were advised to use Personal Protective Equipment (PPE). These findings show that sustained transmission of SARS-CoV-2 among our hospital staff did not occur, beyond the community outbreak, even in the absence of strict infection control measures in non-clinical areas. The results also suggest that current PPE is effective when used appropriately. In addition, our findings emphasise the importance of testing both clinical and non-clinical staff groups during a pandemic.

51. **Seroprevalence of SARS-CoV-2 Antibodies among Healthcare Workers with Differing Levels of COVID-19 Patient Exposure.** Hunter BR, Dbeibo L, Weaver C, et al. *Infect Control Hosp Epidemiol.* 2020 Aug 3:1-7. doi: 10.1017/ice.2020.390. <https://tinyurl.com/y5ae8263>
Findings: Healthcare employees were tested for antibodies against SARS-CoV-2. Among 734 employees, the prevalence of SARS-CoV-2 antibodies was 1.6%. Employees with heavy COVID-19 exposure had similar antibody prevalence as those with limited or no exposure. Guidelines for PPE use seem effective for preventing COVID-19 infection in healthcare workers.

Vaccine

52. **Evaluation of the mRNA-1273 Vaccine against SARS-CoV-2 in Nonhuman Primates.** Corbett KS, Flynn B, Foulds KE, et al. *NEJM.* July 28, 2020 DOI: 10.1056/NEJMoa2024671 <https://www.nejm.org/doi/full/10.1056/NEJMoa2024671?query=TOC>
Findings: Nonhuman primates received 10 or 100 µg of mRNA-1273, a vaccine encoding the prefusion-stabilized spike protein of SARS-CoV-2, or no vaccine. Antibody and T-cell responses were assessed before upper- and lower-airway challenge with SARS-CoV-2. The mRNA-1273 vaccine candidate induced antibody levels exceeding those in human convalescent-phase serum, with live-virus reciprocal 50% inhibitory dilution (ID50) geometric mean titers of 501 in the 10-µg dose group and 3481 in the 100-µg dose group. Vaccination induced type 1 helper T-cell (Th1)-biased CD4 T-cell responses and low or undetectable Th2 or CD8 T-cell responses. Viral replication was not detectable in BAL fluid by day 2 after challenge in seven of eight animals in both vaccinated groups. No viral replication was detectable in the nose of any of the eight animals in the 100-µg dose group by day 2 after challenge, and limited inflammation or detectable viral genome or antigen was noted in lungs of animals in either vaccine group. Vaccination of nonhuman primates with mRNA-1273 induced robust SARS-CoV-2 neutralizing activity, rapid protection in the upper and lower airways, and no pathologic changes in the lung.
53. **ChAdOx1 nCoV-19 vaccine prevents SARS-CoV-2 pneumonia in rhesus macaques.** van Doremalen N, Lambe T, Spencer A, et al. *Nature.* 2020 Jul 30. doi: 10.1038/s41586-020-2608-y. <https://www.nature.com/articles/s41586-020-2608-y>
Findings: Here, we show that the adenovirus-vectored vaccine ChAdOx1 nCoV-19, encoding the spike protein of SARS-CoV-2, is immunogenic in mice, eliciting a robust humoral and cell-

mediated response. This response was predominantly Th1, as demonstrated by IgG subclass and cytokine expression profiling. Vaccination with ChAdOx1 nCoV-19 (prime-only and prime-boost regimen) induced a balanced Th1/Th2 humoral and cellular immune response in rhesus macaques. We observed a significantly reduced viral load in bronchoalveolar lavage fluid and lower respiratory tract tissue of vaccinated rhesus macaques challenged with SARS-CoV-2 compared with control animals, and no pneumonia was observed in vaccinated animals. However, there was no difference in nasal shedding between vaccinated and control animals. Importantly, no evidence of immune-enhanced disease following viral challenge in vaccinated animals was observed. Safety, immunogenicity and efficacy of ChAdOx1 nCoV-19 against symptomatic PCR-positive COVID-19 disease will now be assessed in randomised controlled human clinical trials.

See also: **Single-shot Ad26 vaccine protects against SARS-CoV-2 in rhesus macaques.**

Mercado NB et al. *Nature*. 2020 Jul 30. doi: 10.1038/s41586-020-2607-z.

<https://www.nature.com/articles/s41586-020-2607-z>

Whole Person Care

54. **An audit of end-of-life symptom control in patients with corona virus disease 2019 (COVID-19) dying in a hospital in the United Kingdom.** Alderman B, Webber K, Davies A. *Palliat Med*. 2020 Jul 31:269216320947312. doi: 10.1177/0269216320947312. <https://tinyurl.com/yyxn2x2k>
Findings: The commonest problem was shortness of breath (57.5%), which was generally controlled with conservative doses of morphine (10-20 mg/24 h via a syringe pump). Cough and audible respiratory secretions were relatively uncommon. The second most common problem was agitation/delirium (55.5%), which was generally controlled with standard pharmacological interventions. The cumulative number of patients with shortness of breath, agitation and audible respiratory secretions increased over the last 72 h of life, but most patients were symptom controlled at the point of death. Patients dying of COVID-19 experience similar end-of-life problems to other groups of patients. Moreover, they generally respond to standard interventions for these end-of-life problems.

Women & Children

55. **Are clinical outcomes worse for pregnant women \geq 20 weeks' gestation infected with COVID-19? A multicenter case-control study with propensity score matching.** Badr DA, Mattern J, Carlin A, et al. *Am J Obstet Gynecol*. 2020 Jul 27:S0002-9378(20)30776-6. doi: 10.1016/j.ajog.2020.07.045.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7384420/pdf/main.pdf>
Findings: This propensity score-matched case control study has demonstrated that pregnant women infected with COVID-19 \geq 20 week's gestation, have more severe outcomes than their non-pregnant counterparts. On the basis of this study and that of some other groups, we advise clinicians to exercise prudence when planning the management of pregnant women with COVID-19 infections, particularly in the latter half of the pregnancy, when maternal risk of clinical decompensation and complications may be higher.

56. **Multisystem inflammatory syndrome in children and COVID-19 are distinct presentations of SARS-CoV-2.** Diorio C, Henrickson SE, Vella LA, et al. *J Clin Invest.* 2020 Jul 30:140970. doi: 10.1172/JCI140970. <https://www.jci.org/articles/view/140970/pdf>
Findings: We prospectively enrolled hospitalized patients with evidence of SARS-CoV-2 infection and classified them as having MIS-C or COVID-19. Patients with COVID-19 were classified as having either minimal or severe disease. Twenty patients were enrolled (9 severe COVID-19, 5 minimal COVID-19, and 6 MIS-C). Five cytokines (IFN- γ , IL-10, IL-6, IL-8 and TNF- α) contributed to the analysis. TNF- α and IL-10 discriminated between patients with MIS-C and severe COVID-19. Cts and burr cells on blood smears also differentiated between patients with severe COVID-19 and those with MIS-C. Pediatric patients with SARS-CoV-2 are at risk for critical illness with severe COVID-19 and MIS-C. Cytokine profiling and examination of peripheral blood smears may distinguish between patients with MIS-C and severe COVID-19.
57. **Vertical Transmission of COVID-19: A Systematic Review and Meta-analysis.** Kotlyar A, Grechukhina O, Chen A, et al. *Am J Obstet Gynecol.* 2020 Jul 30:S0002-9378(20)30823-1. doi: 10.1016/j.ajog.2020.07.049. [https://www.ajog.org/article/S0002-9378\(20\)30823-1/pdf](https://www.ajog.org/article/S0002-9378(20)30823-1/pdf)
Findings: Our quantitative synthesis revealed that of 936 neonates from COVID-19 infected mothers, 27 neonates had SARS-CoV-2 viral RNA positive nasopharyngeal swab, indicating a pooled proportion of 3.2% (95% CI 2.2-4.3%) for vertical transmission. Vertical transmission of SARS-CoV-2 is possible and appears to occur in a minority of cases of maternal COVID-19 infection in third trimester. Rates of infection are similar to other pathogens that cause congenital infections. However, given the paucity of early trimester data, no assessment can yet be made regarding rates of vertical transmission in early pregnancy as well as potential risk for consequent fetal morbidity and mortality.
58. **Outcomes of Maternal-Newborn Dyads after Maternal SARS-CoV-2.** Verma S, Bradshaw C, Auyeung NSF, et al. *Pediatrics.* 2020 Jul 31:e2020005637. doi: 10.1542/peds.2020-005637. <https://pediatrics.aappublications.org/content/pediatrics/early/2020/07/29/peds.2020-005637.full.pdf>
Findings: There were a total of 149 mothers with SARS-CoV-2 infection and 149 newborns analyzed (3 sets of twins; 3 stillbirths). Forty percent of these mothers were asymptomatic. Approximately 15% of symptomatic mothers required some form of respiratory support and 8% required intubation. Eighteen newborns (12%) were admitted to the intensive care unit. Fifteen (10%) were born preterm, and five (3%) required mechanical ventilation. Symptomatic mothers had more premature deliveries (16% vs 3%, P= 0.02) and their newborns were more likely to require intensive care (19% vs. 2%, P=0.001) than asymptomatic mothers. One newborn tested positive for SARS-CoV-2, which was considered a case of horizontal postnatal transmission. Although there was no distinct evidence of vertical transmission from mothers with SARS-CoV-2 to their newborns, we did observe perinatal morbidities among both mothers and newborns. Symptomatic mothers were more likely to experience premature delivery and their newborns to require intensive care.

59. **Racial and ethnic disparities in severity of COVID-19 disease in pregnancy in the United States.** Onwuzurike C, Diouf K, Meadows AR, Nour NM. *Int J Gynaecol Obstet.* 2020 Jul 31. doi: 10.1002/ijgo.13333. <https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1002/ijgo.13333?af=R>
Findings: 44 pregnant or recently postpartum women were diagnosed with COVID-19 in our practice by PCR testing. The majority of these patients belonged to racial or ethnic minority groups. Hispanic women represented 48% of the cases and non-Hispanic Black women represented 34% of the cases. This is particularly notable given the clinic patient population is 30% non-Hispanic Black, 30% Hispanic, 20% non-Hispanic White, and 15% Asian. Of the nine women who required hospitalization for COVID-19, eight identified as non-Hispanic Black or Hispanic.

GUIDELINES & CONSENSUS STATEMENTS

[Remdesivir for severe covid-19: a clinical practice guideline.](#) Rochwerg B, Agarwal A, Zeng L, et al. *BMJ* 2020; 370 :m2924

[Update Alert 2: Should Clinicians Use Chloroquine or Hydroxychloroquine Alone or in Combination With Azithromycin for the Prophylaxis or Treatment of COVID-19? Practice Points From the American College of Physicians.](#) Qaseem A, Yost J, Etcheandia-Ikobaltzeta I, Humphrey LL. *Ann Intern Med.* 2020 Jul 30. doi: 10.7326/L20-1007.

[Update Alert 3: Epidemiology of and Risk Factors for Coronavirus Infection in Health Care Workers.](#) Chou R, Dana T, Buckley DI, et al. *Ann Intern Med.* 2020 Aug 3. doi: 10.7326/L20-1005.

[AGA Institute Rapid Review and Recommendations on the Role of Pre-Procedure SARS-CoV2 Testing and Endoscopy.](#) Sultan S, Siddique SM, Altayar O, et al. *Gastroenterology.* 2020 Jul 28:S0016-5085(20)35006-X. doi: 10.1053/j.gastro.2020.07.043.

FDA / CDC / NIH/ WHO Updates

CDC - [Guidance for Healthcare Workers about COVID-19 \(SARS-CoV-2\) Testing](#), updated July 31, 2020

CDC - [Interim Guidelines for COVID-19 Antibody Testing](#), updated August 1, 2020

WHO - [Use of Chest Imaging in the Diagnosis and Management of COVID-19: A WHO Rapid Advice Guide.](#)

WHO - [Preventing and managing COVID-19 across long-term care services: Policy brief, 24 July 2020](#)

Commentary

[COVID-19 and School Closures](#)

[Reopening schools during the COVID-19 pandemic: governments must balance the uncertainty and risks of reopening schools against the clear harms associated with prolonged closure.](#)

[Reopening Primary Schools during the Pandemic](#)

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