

COVID-19 Resource Desk

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New Research

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

Clinical Syndrome

- 1. Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: a nationwide, population-based retrospective cohort study.** Piroth L, Cottenet J, Mariet AS, et al. *Lancet Respir Med.* 2020 Dec 17:S2213-2600(20)30527-0. doi: 10.1016/S2213-2600(20)30527-0. [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30527-0/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30527-0/fulltext)
FINDINGS: 89 530 patients with COVID-19 and 45 819 patients with influenza were hospitalised in France during the respective study periods. In-hospital mortality was higher in patients with COVID-19 than in patients with influenza (15 104 [16·9%] of 89 530 vs 2640 [5·8%] of 45 819), with a relative risk of death of 2·9 (95% CI 2·8-3·0) and an age-standardised mortality ratio of 2·82. Of the patients hospitalised, the proportion of paediatric patients (<18 years) was smaller for COVID-19 than for influenza (1227 [1·4%] vs 8942 [19·5%]), but a larger proportion of patients younger than 5 years needed intensive care support for COVID-19 than for influenza (14 [2·3%] of 613 vs 65 [0·9%] of 6973). In adolescents (11-17 years), the in-hospital mortality was ten-times higher for COVID-19 than for influenza (five [1·1%] of 458 vs one [0·1%] of 804), and patients with COVID-19 were more frequently obese or overweight. The presentation of patients with COVID-19 and seasonal influenza requiring hospitalisation differs considerably. Severe acute respiratory syndrome coronavirus 2 is likely to have a higher potential for respiratory pathogenicity, leading to more respiratory complications and to higher mortality. In children, although the rate of hospitalisation for COVID-19 appears to be lower than for influenza, in-hospital mortality is higher; however, low patient numbers limit this finding. These findings highlight the importance of appropriate preventive measures for COVID-19, as well as the need for a specific vaccine and treatment.
- 2. Comparative evaluation of clinical manifestations and risk of death in patients admitted to hospital with covid-19 and seasonal influenza: cohort study.** Xie Y, Bowe B, Maddukuri G, Al-Aly Z. *BMJ.* 2020 Dec 15;371:m4677. doi: 10.1136/bmj.m4677. <https://www.bmj.com/content/371/bmj.m4677>
Findings: Compared with seasonal influenza, covid-19 was associated with higher risk of acute kidney injury, incident renal replacement therapy, incident insulin use, severe septic shock,

vasopressor use, pulmonary embolism, deep venous thrombosis, stroke, acute myocarditis, arrhythmias and sudden cardiac death, elevated troponin, elevated aspartate aminotransferase, elevated alanine aminotransferase, and rhabdomyolysis. Compared with seasonal influenza, covid-19 was also associated with higher risk of death, mechanical ventilator use, and admission to intensive care and 3.00 additional days of hospital stay. Differences in rates of death per 100 patients between covid-19 and seasonal influenza were most pronounced in people over 75 years of age with chronic kidney disease or dementia and those with black race and obesity, diabetes, or chronic kidney disease. Among people admitted to hospital, compared with seasonal influenza, covid-19 was associated with increased risk of extrapulmonary organ dysfunction, death, and increased health resource use. The findings may inform the global discussion about the comparative risks of covid-19 and seasonal influenza and may help the ongoing effort to manage the covid-19 global pandemic.

3. **The Prevalence of Acute Kidney Injury in Patients Hospitalized With COVID-19 Infection: A Systematic Review and Meta-analysis.** Silver SA, Beaubien-Souligny W, Shah PS, et al. *Kidney Med.* 2020 Dec 9. doi: 10.1016/j.xkme.2020.11.008. [https://www.kidneymedicinejournal.org/article/S2590-0595\(20\)30257-0/fulltext](https://www.kidneymedicinejournal.org/article/S2590-0595(20)30257-0/fulltext)
Findings: Of 2,711 records reviewed, we included 53 published and 1 preprint study in the analysis, which comprised 30,657 hospitalized patients with COVID-19. Data on AKI were available for 30,639 patients (n=54 studies). The pooled prevalence of AKI among patients admitted to the ICU was 46% and 19% of all ICU patients with COVID-19 commenced KRT. AKI complicated the course of nearly 1 in 3 patients hospitalized with COVID-19. The risk of AKI was higher in critically ill patients with a substantial number receiving KRT at rates higher than the general ICU population. Since COVID-19 will be a public health threat for the foreseeable future, these estimates should help guide KRT resource planning.
4. **Pulmonary Embolism and Deep Vein Thrombosis in COVID-19: A Systematic Review and Meta-Analysis.** Suh YJ, Hong H, Ohana M, et al. *Radiology.* 2020 Dec 15:203557. doi: 10.1148/radiol.2020203557. <https://pubs.rsna.org/doi/10.1148/radiol.2020203557>
Findings: Twenty-seven studies with 3342 patients with COVID-19 were included in the analysis. The pooled incidence rates of PE and DVT were 16.5% and 14.8%, respectively. PE was more frequently found in patients who were admitted to the ICU (24.7% vs 10.5% in those not admitted to the ICU) and in studies with universal screening using CT pulmonary angiography. DVT was present in 42.4% of patients with PE. D-dimer tests had an area under the receiver operating characteristic curve of 0.737 for PE, and D-dimer levels of 500 and 1000 µg/L showed high sensitivity (96% and 91%, respectively) but low specificity (10% and 24%, respectively). PE and DVT occurred in 16.5% and 14.8% of patients with COVID-19, respectively, and more than half of patients with PE lacked DVT. The cutoffs of D-dimer levels used to exclude PE in preexisting guidelines seem applicable to patients with COVID-19.
5. **Risk and Management of Venous Thromboembolism in Patients with COVID-19.** Skeik N, Smith JE, Patel L, et al. *Ann Vasc Surg.* 2020 Dec 14:S0890-5096(20)31039-6. doi: 10.1016/j.avsg.2020.11.007. <https://www.clinicalkey.com/#!/content/journal/1-s2.0-S0890509620310396>

Findings: While a significant VTE risk has been confirmed in patients with COVID-19, literature addressing best ways to mitigate this risk is lacking. Furthermore, there has been very limited guidance provided by societal guidelines to help prevent and manage VTE associated with the COVID-19 infection. In light of the available data, we advise that all patients admitted with suspected or confirmed COVID-19 receive pharmacological prophylaxis if bleeding risk is acceptable. For patients with COVID-19 who have been discharged from the emergency department or hospital, we suggest extended thromboprophylaxis (up to 39 days) as long as bleeding risk is low. More research is needed to standardize prophylaxis and management protocols for these patients.

6. **Prevalence of Headache in Patients with Coronavirus Disease 2019 (COVID-19): A Systematic Review and Meta-Analysis of 14,275 Patients.** Islam MA, Alam SS, Kundu S, et al. *Front Neurol.* 2020 Nov 27;11:562634. doi: 10.3389/fneur.2020.562634. eCollection 2020.

<https://www.frontiersin.org/articles/10.3389/fneur.2020.562634/full>

Findings: We identified 2,055 studies, of which 86 studies (n = 14,275, 49.4% female) were included in the meta-analysis. Overall, the pooled prevalence of headache in COVID-19 patients was 10.1%. There was no significant difference of headache prevalence in severe or critical vs. non-severe, survived vs. non-survived, and ICU vs. non-ICU COVID-19 patients. From the first 4-month data of the outbreak, headache was detected in 10.1% of the adult COVID-19 patients.

7. **Stroke as a Neurological Complication of COVID-19: A Systematic Review and Meta-Analysis of Incidence, Outcomes and Predictors.** Siow I, Lee KS, Zhang JJY, et al. *J Stroke Cerebrovasc Dis.* 2020 Dec 15;30(3):105549. doi: 10.1016/j.jstrokecerebrovasdis.2020.105549.

<https://www.sciencedirect.com/science/article/pii/S1052305720309678?via%3Dihub>

Findings: 326 studies were screened, and 30 studies reporting findings from 55,176 patients including 899 with stroke were included. The average age of patients who suffered from stroke as a complication of COVID-19 was 65.5 (Range: 40.4-76.4 years). The average incidence of stroke as a complication of COVID-19 was 1.74%. The average mortality of stroke in COVID-19 patients was 31.76%. These patients also had deranged clinical parameters including deranged coagulation profiles, liver function tests, and full blood counts. Although stroke is an uncommon complication of COVID-19, when present, it often results in significant morbidity and mortality. In COVID-19 patients, stroke was associated with older age, comorbidities, and severe illness.

Diagnosics & Screening

8. **Analytical Sensitivity of the Abbott BinaxNOW COVID-19 Ag CARD.** Perchetti GA, Huang ML, Mills MG, et al. *J Clin Microbiol.* 2020 Dec 11;JCM.02880-20. doi: 10.1128/JCM.02880-20.

<https://jcm.asm.org/content/early/2020/12/11/JCM.02880-20>

Findings: Multiple rapid antigen tests for SARS-CoV-2 have recently received Emergency Use Authorization from the United States FDA. Although less sensitive than molecular detection methods, rapid antigen testing offers the potential for cheap, quick, decentralized testing. Here, we evaluated the analytical sensitivity of Abbott BinaxNOW COVID-19 Ag CARD using SARS-CoV-2 positive clinical specimens quantified by RT-ddPCR and multiple FDA EUA qRT-PCR platforms

using RNA standards. Initial and confirmatory limits of detection for the BinaxNOW COVID-19 Ag CARD were determined to be equivalent to 4.04 - 8.06x10⁴ copies/swab. We further confirmed this limit of detection with 72 additional clinical samples positive for SARS-CoV-2 in either phosphate-buffered saline or viral transport media. 100% of samples with viral loads >40,000 copies/swab were detected by rapid antigen testing. These data indicate that the BinaxNOW COVID-19 Ag CARD has the approximate analytical sensitivity equivalent to a generic qRT-PCR CT of 29-30.

9. **Comparison of Rapid Antigen Tests for COVID-19.** Yamayoshi S, Sakai-Tagawa Y, Koga M, et al. *Viruses*. 2020 Dec 10;12(12):E1420. doi: 10.3390/v12121420. <https://www.mdpi.com/1999-4915/12/12/1420>

Findings: RT-qPCR-based tests are widely used to diagnose COVID-19. As a result that these tests cannot be done in local clinics where RT-qPCR testing capability is lacking, rapid antigen tests (RATs) for COVID-19 based on lateral flow immunoassays are used for rapid diagnosis. However, their sensitivity compared with each other and with RT-qPCR and infectious virus isolation has not been examined. Here, we compared the sensitivity among four RATs by using severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) isolates and several types of COVID-19 patient specimens and compared their sensitivity with that of RT-qPCR and infectious virus isolation. Although the RATs read the samples containing large amounts of virus as positive, even the most sensitive RAT read the samples containing small amounts of virus as negative. Moreover, all RATs tested failed to detect viral antigens in several specimens from which the virus was isolated. The current RATs will likely miss some COVID-19 patients who are shedding infectious SARS-CoV-2.

Epidemiology & Public Health

10. **COVID-19 as the Leading Cause of Death in the United States.** Woolf SH, Chapman DA, Lee JH. *JAMA*. December 17, 2020. doi:10.1001/jama.2020.24865 <https://jamanetwork.com/journals/jama/fullarticle/2774465>

Findings: A helpful approach to put the effects of the pandemic in context is to compare COVID-19–related mortality rates with the leading causes of death that, under ordinary circumstances, would pose the greatest threat to different age groups. The conditions listed include the 3 leading causes of death in each of the 10 age groups from infancy to old age. Using data from the Centers for Disease Control and Prevention, we show mortality rates for these conditions during the period of March through October 2018 (the most recent year for which detailed cause-of-death data are available) with COVID-19 mortality rates during March through October 2020. Data shows that by October 2020 COVID-19 had become the third leading cause of death for persons aged 45 through 84 years and the second leading cause of death for those aged 85 years or older. Adults 45 years or older were more likely to die from COVID-19 during those months than from chronic lower respiratory disease, transport accidents (eg, motor vehicle fatalities), drug overdoses, suicide, or homicide. In contrast, for individuals younger than age 45 years, other causes of death, such as drug overdoses, suicide, transport accidents, cancer, and homicide exceeded those from COVID-19.

- 11. All-Cause Excess Mortality and COVID-19-Related Mortality Among US Adults Aged 25-44 Years, March-July 2020.** Faust JS, Krumholz HM, Du C, et al. *JAMA*. 2020 Dec 16. doi: 10.1001/jama.2020.24243. <https://jamanetwork.com/journals/jama/fullarticle/2774445>
Findings: The COVID-19 pandemic was associated with increases in all-cause mortality among US adults aged 25 to 44 years from March through July of 2020. In 3 HHS regions, COVID-19 deaths were similar to or exceeded unintentional opioid overdoses that occurred during several corresponding months of 2018. Only 38% of all-cause excess deaths in adults aged 25 to 44 years recorded during the pandemic were attributed directly to COVID-19. Although the remaining excess deaths are unexplained, inadequate testing in this otherwise healthy demographic likely contributed. These results suggest that COVID-19–related mortality may have been underdetected in this population.
- 12. Excess Mortality in California during the Coronavirus Disease 2019 Pandemic, March to August 2020.** Chen YH, Glymour MM, Catalano R, et al. *JAMA Intern Med*. 2020 Dec 21. doi: 10.1001/jamainternmed.2020.7578. <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2774273>
Findings: From March 1 through August 22, 2020, 146 557 deaths were recorded in California, with an estimated 19 806 deaths in excess of those predicted by historical trends. Older adults, Black and Latino residents, and those without college degrees have experienced the highest per capita excess mortality. Following the statewide shelter-in-place, Latino residents and those without a high school degree/GED had the greatest increase in excess per capita mortality, with rates more than tripling after reopening. We hypothesize that this pattern reflects the risk of COVID-19 death faced by low-wage, essential workers and their social networks owing to occupational exposure, crowded housing, and inadequate access to testing or treatments.
- 13. Global evidence for ultraviolet radiation decreasing COVID-19 growth rates.** Carleton T, Cornetet J, Huybers P, Meng KC, Proctor J. *Proc Natl Acad Sci U S A*. 2021 Jan 7;118(1):e2012370118. doi: 10.1073/pnas.2012370118. <https://www.pnas.org/content/118/1/e2012370118.long>
Findings: We combine a spatially resolved dataset of confirmed COVID-19 cases, composed of 3,235 regions across 173 countries, with local environmental conditions and a statistical approach developed to quantify causal effects of environmental conditions in observational data settings. We find that UV radiation has a statistically significant effect on daily COVID-19 growth rates: a SD increase in UV lowers the daily growth rate of COVID-19 cases by 1 percentage point over the subsequent 2.5 wk, relative to an average in-sample growth rate of 13.2%. The time pattern of lagged effects peaks 9 to 11 d after UV exposure, consistent with the combined timescale of incubation, testing, and reporting. Cumulative effects of temperature and humidity are not statistically significant. Simulations illustrate how seasonal changes in UV have influenced regional patterns of COVID-19 growth rates from January to June, indicating that UV has a substantially smaller effect on the spread of the disease than social distancing policies. Furthermore, total COVID-19 seasonality has indeterminate sign for most regions during this period due to uncertain effects of other environmental variables. Our findings indicate UV exposure influences COVID-19 cases, but a comprehensive understanding of seasonality awaits further analysis.

14. **Impacts of the COVID-19 pandemic on rural America.** Mueller JT, McConnell K, Burow PB, et al. *Proc Natl Acad Sci U S A*. 2021 Jan 5;118(1):2019378118. doi: 10.1073/pnas.2019378118.

<https://www.pnas.org/content/118/1/2019378118>

Findings: Data from a new survey was designed to assess the impacts of the pandemic on health-related and economic dimensions of rural well-being in the North American West. Notably, we find that the effects of the COVID-19 pandemic on rural populations have been severe, with significant negative impacts on unemployment, overall life satisfaction, mental health, and economic outlook. Further, we find that these impacts have been generally consistent across age, ethnicity, education, and sex. We discuss how these findings constitute the beginning of a much larger interdisciplinary COVID-19 research effort that integrates rural areas and pushes beyond the predominant focus on cities and nation-states.

Healthcare Delivery & Healthcare Workers

15. **Managing intensive care admissions when there are not enough beds during the COVID-19 pandemic: a systematic review.** Tyrrell CSB, Mytton OT, Gentry SV, et al. *Thorax*. 2020 Dec 17;thoraxjnl-2020-215518. doi: 10.1136/thoraxjnl-2020-215518.

<https://thorax.bmj.com/content/early/2020/12/16/thoraxjnl-2020-215518>

Findings: To understand how to manage which patients are admitted to ICU, and receive mechanical ventilatory support, during periods of high demand during the COVID-19 pandemic, a systematic review was performed. Six guidelines were national or transnational level guidance (UK, Switzerland, Belgium, Australia and New Zealand, Italy, and Sri Lanka), with one state level (Kansas, USA), one international (Extracorporeal Life Support Organization) and one specific to military hospitals (Department of Defense, USA). The guidelines covered several broad themes: use of ethical frameworks, criteria for ICU admission and discharge, adaptation of criteria as demand changes, equality across health conditions and healthcare systems, decision-making processes, communication of decisions, and guideline development processes. We have synthesised the current guidelines and identified the different approaches taken globally to manage the triage of intensive care resources during the COVID-19 pandemic. There is limited consensus on how to allocate the finite resource of ICU beds and ventilators, and a lack of high-quality evidence and guidelines on resource allocation during the pandemic. We have developed a set of factors to consider when developing guidelines for managing intensive care admissions and outlined implications for clinical leads and local implementation.

16. **Care bundles for improving outcomes in patients with COVID-19 or related conditions in intensive care - a rapid scoping review.** Smith V, Devane D, Nichol A, Roche D. *Cochrane Database Syst Rev*. 2020 Dec 21;12:CD013819. doi: 10.1002/14651858.CD013819.

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.cd013819/full>

Findings: This scoping review has identified 21 studies on care bundle use in critically ill patients in ICU with COVID-19, ARDS, viral influenza or pneumonia and severe respiratory failure. The data for patients with COVID-19 specifically are limited, derived mainly from observational quality improvement or clinical experiential accounts. Research is required, urgently, to further assess care bundle use and optimal components of these bundles in this patient cohort. The

care bundles described were also varied, with guidance on ventilator settings described in 10 care bundles, while chest X-ray was part mentioned in one care bundle in one study only. None of the studies identified in this scoping review measured users' experience of adapting care bundles. Optimising care bundle implementation requires that the components of the care bundle are collectively and consistently applied. Data on challenges, barriers and facilitators to implementation are needed. A formal synthesis of the outcome data presented in this review and a critical appraisal of the evidence is required by a subsequent effectiveness review. This subsequent review should further explore effect estimates across the included studies.

Laboratory Results

- 17. Persistence of IgG response to SARS-CoV-2.** Duysburgh E, Mortgat L, Barbezange C, et al. *Lancet Infect Dis.* 2020 Dec 17:S1473-3099(20)30943-9. doi: 10.1016/S1473-3099(20)30943-9. [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30943-9/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30943-9/fulltext)
Findings: Since April 22, 2020, we have been following up a representative cohort of 850 health-care workers from 17 Belgian hospitals. Participants are tested on a monthly basis for the presence of SARS-CoV-2 with quantitative RT-PCR and for antibodies targeting S1 protein with a commercial semi-quantitative ELISA, using a stringent manufacturer-defined cut-off for having a positive test result. By the end of September, 2020, 81 IgG-positive health-care workers had been identified. Of these individuals, five were asymptomatic, 75 had reported mild symptoms, and one needed hospitalisation. Median follow-up was 170 (range 62–199) days. In seven (9%) health-care workers, antibodies became undetectable after intervals ranging from 107 days to 159 days from presumed onset of infection (defined by day of positive RT-qPCR test or [if not available] day of onset of symptoms or [for asymptomatic patients] day of first positive serological test minus 14 days). Among 74 (91%) health-care workers who remained seropositive, median duration of antibody persistence (defined as the time between the day IgGs were last detected and the day of presumed onset of infection) is currently 168.5 (range 62–199) days. 71 (96%) of 74 health-care workers have already had antibodies for 90 days or more and 67 (91%) have had them for 120 days or more.

Prognosis

- 18. Variation in US Hospital Mortality Rates for Patients Admitted With COVID-19 During the First 6 Months of the Pandemic.** Asch DA, Sheils NE, Islam N, et al. *JAMA Intern Med.* December 22, 2020. doi:10.1001/jamainternmed.2020.8193
<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2774572?resultClick=1>
Findings: It is unknown how much the mortality of patients with COVID-19 depends on the hospital that cares for them, and whether COVID-19 hospital mortality rates are improving. This cohort study assessed 38 517 adults who were admitted with COVID-19 to 955 US hospitals from January 1, 2020, to June 30, 2020, and a subset of 27 801 adults (72.2%) who were admitted to 398 of these hospitals that treated at least 10 patients with COVID-19 during 2 periods (January 1 to April 30, 2020, and May 1 to June 30, 2020). The mean age among participants (18 888 men [49.0%]) was 70.2 years. The mean hospital-level risk-standardized event rate (RSER) for the 955 hospitals was 11.8%. The mean RSER in the worst-performing

quintile of hospitals was 15.65% compared with 9.06% in the best-performing quintile. Mean RSERs in all but 1 of the 398 hospitals improved. Over the first months of the pandemic, COVID-19 mortality rates in this cohort of US hospitals declined. Hospitals did better when the prevalence of COVID-19 in their surrounding communities was lower.

19. **The association between blood pressure control and Coronavirus Disease 2019 outcomes in 45,418 symptomatic patients with hypertension: An observational cohort study.** Sheppard JP, Nicholson B, Lee J, et al. *Hypertension*. 2020 Dec 16. doi: 10.1161/HYPERTENSIONAHA.120.16472.

<https://www.ahajournals.org/doi/abs/10.1161/HYPERTENSIONAHA.120.16472>

Findings: Of the 45,418 patients (mean age 67 years; 44.7% male) included, 11,950 (26.3%) had controlled BP. These patients were older, had more co-morbidities and had been diagnosed with hypertension for longer. A total of 4,277 patients (9.4%) were diagnosed with COVID-19 and 877 died within 28 days. Individuals with stage 1 uncontrolled BP had lower odds of COVID-19 death (OR 0.76, 95%CI 0.62-0.92) compared to patients with well-controlled BP. There was no association between BP control and COVID-19 diagnosis or hospitalisation. These findings suggest BP control may be associated with worse COVID-19 outcomes, possibly due to these patients having more advanced atherosclerosis and target organ damage. Such patients may need to consider adhering to stricter social-distancing, to limit the impact of COVID-19 as future waves of the pandemic occur.

20. **Association between Achieving Inpatient Glycemic Control and Clinical Outcomes in Hospitalized Patients With COVID-19: A Multicenter, Retrospective Hospital-Based Analysis.** Klonoff DC, Messler JC, Umpierrez GE, et al. *Diabetes Care*. 2020 Dec 15:dc201857. doi: 10.2337/dc20-1857. <https://care.diabetesjournals.org/content/early/2020/12/08/dc20-1857.full-text.pdf>

Findings: Overall, 18.1% (279/1,544) of patients died in the hospital. In non-ICU patients, severe hyperglycemia (blood glucose [BG] >13.88 mmol/L [250 mg/dL]) on days 2-3 was independently associated with high mortality compared with patients with BG <7.77 mmol/L (140 mg/dL). This relationship was not significant for admission glucose (HR 1.465; 95% CI 0.683-3.143). In patients admitted directly to the ICU, severe hyperglycemia on admission was associated with increased mortality. This relationship was not significant on day 2. Hypoglycemia (BG <70 mg/dL) was also associated with increased mortality. Both hyperglycemia and hypoglycemia were associated with poor outcomes in patients with COVID-19. Admission glucose was a strong predictor of death among patients directly admitted to the ICU. Severe hyperglycemia after admission was a strong predictor of death among non-ICU patients.

21. **Impact of COVID-19 in patients with concurrent co-infections: a systematic review and meta-analyses.** Sarkar S, Khanna P, Singh AK. *J Med Virol*. 2020 Dec 17. doi: 10.1002/jmv.26740. <https://onlinelibrary.wiley.com/doi/10.1002/jmv.26740>

Findings: Our search retrieved 20 studies, with a total of 205,702 patients. Patients with Tuberculosis & Influenza have an increased risk of mortality during a co-infection with SARS-CoV-2. No significant impact is found in people living with HIV or Chronic hepatitis. Several countries (Brazil, Paraguay, Argentina, Peru, Colombia, and Singapore) are on the verge of a

Dengue co epidemic (cumulative 878496 and 5028380 cases of Dengue and Covid-19 respectively) CONCLUSIONS: The impact of COVID-19 in patients of concurrent infections with either Tuberculosis or Influenza is detrimental. The clinical outcomes of COVID-19 in HIV or Chronic hepatitis patients are comparable to COVID-19 patients without these concurrent infections.

22. **Prognostic Impact of Hyponatremia and Hypernatremia in COVID-19 Pneumonia. A HOPE-COVID-19 (Health Outcome Predictive Evaluation for COVID-19) Registry Analysis.** HOPE COVID-19 investigators. *Front Endocrinol (Lausanne)*. 2020 Nov 30;11:599255. doi:10.3389/fendo.2020.599255. eCollection 2020.

<https://www.frontiersin.org/articles/10.3389/fendo.2020.599255/full>

Findings: The aim of this study was to ascertain whether admittance dysnatremia is associated with mortality, sepsis, or intensive therapy (IT) in patients hospitalized with SARS-COV2 pneumonia. This is a retrospective study of the HOPE-COVID-19 registry, with data collected from January 1th through April 31th, 2020. Patients were classified as hyponatremic (SNa <135 mmol/L), eunatremic (SNa 135-145 mmol/L), or hypernatremic (SNa >145 mmol/L). Four thousand six hundred sixty-four patients were analyzed, median age 66 (52-77), 58% males. Death occurred in 988 (21.2%) patients, sepsis was diagnosed in 551 (12%) and IT in 838 (18.4%). Hyponatremia was present in 957/4,664 (20.5%) patients, and hypernatremia in 174/4,664 (3.7%). Both hyponatremia and hypernatremia were associated with mortality and sepsis. Only hyponatremia was associated with IT. In conclusion, hyponatremia and hypernatremia at admission are factors independently associated with mortality and sepsis in patients hospitalized with SARS-COV2 pneumonia.

23. **Impact of Sex and Metabolic Comorbidities on COVID-19 Mortality Risk Across Age Groups: 66,646 Inpatients Across 613 U.S. Hospitals.** Goodman KE, Magder LS, Baghdadi JD, et al. *Clin Infect Dis*. 2020 Dec 18:ciaa1787. doi: 10.1093/cid/ciaa1787.

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1787/6041643>

Findings: Among 66,646 (6.5%) admissions with a COVID-19 diagnosis, across 613 U.S. hospitals, 12,388 (18.6%) died in-hospital. In multivariable analysis, male sex was independently associated with 30% higher mortality risk. Diabetes without chronic complications was not a risk factor at any age, and hypertension without chronic complications was only a risk factor in 20-39 year-olds. Diabetes with chronic complications, hypertension with chronic complications, and obesity were risk factors in most age-groups, with highest relative risks among 20-39 year-olds. Hospitalized men with COVID-19 are at increased risk of death across all ages. Hypertension, diabetes with chronic complications, and obesity demonstrated age-dependent effects, with the highest relative risks among adults aged 20-39.

24. **Absolute Lymphocytes, Ferritin, C-Reactive Protein, and Lactate Dehydrogenase Predict Early Invasive Ventilation in Patients With COVID-19.** Payán-Pernía S, Gómez Pérez L, Remacha Sevilla ÁF, et al. *Lab Med*. 2020 Dec 18:Imaa105. doi: 10.1093/labmed/Imaa105.

<https://academic.oup.com/labmed/advance-article/doi/10.1093/labmed/Imaa105/6041251>

Findings: In this single-center retrospective observational study, we aimed to identify simple laboratory parameters that in combination with ferritin (a surrogate marker of severe

inflammation) may help predict early (first 48 hours) MIV. A total of 160 patients with COVID-19 in whom serum ferritin, absolute lymphocyte count (ALC), platelet count, C-reactive protein (CRP), and lactate dehydrogenase (LDH) had been analyzed at admission were included. We found that ferritin, LDH, ALC, and CRP predicted with 88% accuracy the probability of early MIV. Results indicated that LDH showed the greater area under the curve (AUC), with a value of 89.1%. Using the AUC, we established cutoff values for clinical application. Finally, we developed a classification tree based on LDH for its clinical use. Ferritin, LDH, ALC, and CRP predict with 88% accuracy the probability of early MIV.

25. **Impact of cardiovascular disease and risk factors on fatal outcomes in patients with COVID-19 according to age: a systematic review and meta-analysis.** Bae S, Kim SR, Kim MN, et al. *Heart*. 2020 Dec 17;heartjnl-2020-317901. doi: 10.1136/heartjnl-2020-317901.

<https://heart.bmj.com/content/early/2020/12/16/heartjnl-2020-317901>

Findings: We included 51 studies with a total of 48 317 patients with confirmed COVID-19 infection. Overall, the relative risk of developing severe COVID-19 or death was significantly higher in patients with risk factors for CVD (hypertension: OR 2.50, 95% CI 2.15 to 2.90; diabetes: 2.25, 95% CI 1.89 to 2.69) and CVD (3.11, 95% 2.55 to 3.79). Younger patients had a lower prevalence of hypertension, diabetes and CVD compared with older patients; however, the relative risk of fatal outcomes was higher among the former. The results of the meta-analysis suggest that CVD and its risk factors (hypertension and diabetes) were closely related to fatal outcomes in COVID-19 for patients across all ages. Although young patients had lower prevalence rates of cardiovascular comorbidities than elderly patients, relative risk of fatal outcome in young patients with hypertension, diabetes and CVD was higher than in elderly patients.

26. **Derivation and validation of a prognostic model for predicting in-hospital mortality in patients admitted with COVID-19 in Wuhan, China: the PLANS (platelet lymphocyte age neutrophil sex) model.** Li J, Chen Y, Chen S, et al. *BMC Infect Dis*. 2020 Dec 17;20(1):959. doi: 10.1186/s12879-020-05688-y.

<https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-020-05688-y>

Findings: The final model (PLANS), including five predictor variables of platelet count, lymphocyte count, age, neutrophil count, and sex, had an excellent predictive performance. Internal validation showed little overfitting. External validation using an independent cohort (47.8% female, median age 63) demonstrated excellent predictive performance (C-index: 0.87, 95% CI: 0.85 to 0.89; calibration slope: 1.02, 95% CI: 0.92 to 1.12). The averaged predicted cumulative incidence curves were close to the observed cumulative incidence curves in patients with different risk profiles. The PLANS model based on five routinely collected predictors would assist clinicians in better triaging patients and allocating healthcare resources to reduce COVID-19 fatality.

27. **Pre-existing COPD is associated with an increased risk of mortality and severity in COVID-19: a rapid systematic review and meta-analysis.** Rabbani G, Shariful Islam SM, Rahman MA, et al. *Expert Rev Respir Med*. 2020 Dec 17. doi: 10.1080/17476348.2021.1866547.

<https://www.tandfonline.com/doi/full/10.1080/17476348.2021.1866547>

Findings: Our meta-analysis showed an increased likelihood of mortality in COVID-19 patients with pre-existing COPD. Furthermore, pooled estimate for the association between pre-existing COPD and severity due to COVID-19 was also significant. Males had an increased risk of mortality compared to females. We found that patients with pre-existing COPD had more than three times higher risk of mortality and severe COVID-19. There is a need to identify patients with pre-existing COPD during the pandemic so that early interventions can be aimed for this group of patients.

28. **Association of liver abnormalities with in-hospital mortality in patients with COVID-19.** Tongji Multidisciplinary Team for Treating COVID-19 (TTTC). *J Hepatol.* 2020 Dec 18:S0168-8278(20)33885-X. doi: 10.1016/j.jhep.2020.12.012. [https://www.journal-of-hepatology.eu/article/S0168-8278\(20\)33885-X/pdf](https://www.journal-of-hepatology.eu/article/S0168-8278(20)33885-X/pdf)

Findings: Abnormal AST and D-Bil levels at admission were independent predictors of COVID-19 mortality. Therefore, monitoring liver chemistries, especially AST and D-Bil levels, in hospitalized patients with COVID-19, is necessary.

Survivorship & Rehabilitation

29. **Persistent symptoms after Covid-19: qualitative study of 114 "long Covid" patients and draft quality principles for services.** Ladds E, Rushforth A, Wieringa S, et al. *BMC Health Serv Res.* 2020 Dec 20;20(1):1144. doi: 10.1186/s12913-020-06001-y. <https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-020-06001-y>

Findings: Of 114 participants aged 27-73 years, 80 were female. Eighty-four were White British, 13 Asian, 8 White Other, 5 Black, and 4 mixed ethnicity. Thirty-two were doctors and 19 other health professionals. Thirty-one had attended hospital, of whom 8 had been admitted. Analysis revealed a confusing illness with many, varied and often relapsing-remitting symptoms and uncertain prognosis; a heavy sense of loss and stigma; difficulty accessing and navigating services; difficulty being taken seriously and achieving a diagnosis; disjointed and siloed care (including inability to access specialist services); variation in standards (e.g. inconsistent criteria for seeing, investigating and referring patients); variable quality of the therapeutic relationship (some participants felt well supported while others felt "fobbed off"); and possible critical events (e.g. deterioration after being unable to access services). Emotionally significant aspects of participants' experiences informed ideas for improving services. Suggested quality principles for a long Covid service include ensuring access to care, reducing burden of illness, taking clinical responsibility and providing continuity of care, multi-disciplinary rehabilitation, evidence-based investigation and management, and further development of the knowledge base and clinical services.

30. **High Prevalence of Pulmonary Sequelae at 3 Months After Hospital Discharge in Mechanically Ventilated COVID-19 Survivors.** van Gassel RJJ, Bels JLM, Raafs A, et al. *Am J Respir Crit Care Med.* 2020 Dec 16. doi: 10.1164/rccm.202010-3823LE. <https://www.atsjournals.org/doi/abs/10.1164/rccm.202010-3823LE>

Findings: The majority of invasive mechanically ventilated COVID-19 survivors still had abnormal pulmonary function tests and residual changes on HRCT at three months after hospital

discharge. Diminished diffusion capacity, total lung capacity, and fibrosis on HRCT were the dominant features. Our findings warrant intensive respiratory follow-up of mechanically ventilated COVID-19 patients.

31. **Increased care at discharge from COVID-19: The association between pre-admission frailty and increased care needs after hospital discharge; a multicentre European observational cohort study.** Vilches-Moraga A, Price A, Braude P, et al. *BMC Med.* 2020 Dec 18;18(1):408. doi: 10.1186/s12916-020-01856-8. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7746415/>
Findings: Around a quarter of patients admitted with COVID-19 had increased care needs at discharge. Pre-admission frailty was strongly associated with the need for an increased level of care at discharge. Our results have implications for service planning and public health policy as well as a person's functional outcome, suggesting that frailty screening should be utilised for predictive modelling and early individualised discharge planning.

Therapeutics

32. **Corticosteroid use in COVID-19 patients: a systematic review and meta-analysis on clinical outcomes.** van Paassen J, Vos JS, Hoekstra EM, Neumann KMI, Boot PC, Arbous SM. *Crit Care.* 2020 Dec 14;24(1):696. doi: 10.1186/s13054-020-03400-9. <https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-03400-9>
Findings: Forty-four studies were included, covering 20,197 patients. In twenty-two studies, the effect of corticosteroid use on mortality was quantified. The overall pooled estimate (observational studies and RCTs) showed a significant reduced mortality in the corticosteroid group. Furthermore, viral clearance time ranged from 10 to 29 days in the corticosteroid group and from 8 to 24 days in the standard of care group. Fourteen studies reported a positive effect of corticosteroids on need for and duration of mechanical ventilation. A trend toward more infections and antibiotic use was present. Our findings from both observational studies and RCTs confirm a beneficial effect of corticosteroids on short-term mortality and a reduction in need for mechanical ventilation. And although data in the studies were too sparse to draw any firm conclusions, there might be a signal of delayed viral clearance and an increase in secondary infections.
33. **Barotrauma in mechanically-ventilated patients with coronavirus disease 2019: a survey of 38 hospitals in Lombardy, Italy.** Protti A, Greco M, Filippini M, et al. *Minerva Anesthesiol.* 2020 Dec 16. doi: 10.23736/S0375-9393.20.15002-8. <https://www.minervamedica.it/en/journals/minerva-anestesiologica/article.php?cod=R02Y9999N00A20121605>
Findings: The study was an electronic survey open from March 27th to May 2nd, 2020. Patients with COVID-19 who developed barotrauma while on invasive mechanical ventilation from 61 hospitals of the COVID-19 Lombardy Intensive Care Unit Network were involved. The response rate was 38/61 (62%). The incidence of barotrauma was 145/2041 (7.1%). Only a few cases occurred with ventilatory settings that may be considered non-protective such as a plateau airway pressure >35 cmH₂O (2/113 [2%]), a driving airway pressure >15 cmH₂O (30/113 [27%]), or a tidal volume >8 ml/kg of ideal body weight and a plateau airway pressure >30 cmH₂O

(12/134 [9%]). Within the limits of a survey, patients with COVID-19 might be at high risk for barotrauma during invasive (and allegedly lung-protective) mechanical ventilation.

34. **Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia.** Salama C, Han J, Yau L, et al. *N Engl J Med.* 2020 Dec 17. doi: 10.1056/NEJMoa2030340.

<https://www.nejm.org/doi/full/10.1056/NEJMoa2030340>

Findings: We randomly assigned (in a 2:1 ratio) patients hospitalized with Covid-19 pneumonia who were not receiving mechanical ventilation to receive standard care plus one or two doses of either tocilizumab (8 mg per kilogram of body weight intravenously) or placebo. A total of 389 patients underwent randomization, and the modified intention-to-treat population included 249 patients in the tocilizumab group and 128 patients in the placebo group; 56.0% were Hispanic or Latino, 14.9% were Black, 12.7% were American Indian or Alaska Native, 12.7% were non-Hispanic White, and 3.7% were of other or unknown race or ethnic group. The cumulative percentage of patients who had received mechanical ventilation or who had died by day 28 was 12.0% in the tocilizumab group and 19.3% in the placebo group. Death from any cause by day 28 occurred in 10.4% of the patients in the tocilizumab group and 8.6% of those in the placebo group. In the safety population, serious adverse events occurred in 38 of 250 patients (15.2%) in the tocilizumab group and 25 of 127 patients (19.7%) in the placebo group. In hospitalized patients with Covid-19 pneumonia who were not receiving mechanical ventilation, tocilizumab reduced the likelihood of progression to the composite outcome of mechanical ventilation or death, but it did not improve survival. No new safety signals were identified.

35. **REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19.** Weinreich DM, Sivapalasingam S, Norton T, et al. *N Engl J Med.* 2020 Dec 17. doi: 10.1056/NEJMoa2035002.

<https://www.nejm.org/doi/full/10.1056/NEJMoa2035002>

Findings: In this ongoing, double-blind, phase 1-3 trial involving nonhospitalized patients with Covid-19, we investigated two fully human, neutralizing monoclonal antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein, used in a combined cocktail (REGN-COV2) to reduce the risk of the emergence of treatment-resistant mutant virus. Patients were randomly assigned (1:1:1) to receive placebo, 2.4 g of REGN-COV2, or 8.0 g of REGN-COV2 and were prospectively characterized at baseline for endogenous immune response against SARS-CoV-2. Data from 275 patients are reported. In this interim analysis, the REGN-COV2 antibody cocktail reduced viral load, with a greater effect in patients whose immune response had not yet been initiated or who had a high viral load at baseline. Safety outcomes were similar in the combined REGN-COV2 dose groups and the placebo group.

36. **Early Outcomes from Early Tracheostomy for Patients with COVID-19.** Kwak PE, Connors JR, Benedict PA, et al. *JAMA Otolaryngol Head Neck Surg.* 2020 Dec 17. doi: 10.1001/jamaoto.2020.4837.

<https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2774263>

Findings: This cohort study from the first 2 months of the pandemic in New York City provides an opportunity to reconsider guidelines for tracheostomy for patients with COVID-19. Findings demonstrated noninferiority of early tracheostomy and challenges recommendations to

categorically delay or avoid tracheostomy in this patient population. When aligned with emerging evidence about the timeline of infectivity of the novel coronavirus, this approach may optimize outcomes from tracheostomy while keeping clinicians safe.

37. **Thromboprophylaxis (sic) with Fondaparinux vs. Enoxaparin in Hospitalized COVID-19 Patients: A Multicenter Italian Observational Study.** Russo V, Cardillo G, Viggiano GV, et al. *Front Med (Lausanne)*. 2020 Nov 27;7:569567. doi: 10.3389/fmed.2020.569567. eCollection 2020. <https://www.frontiersin.org/articles/10.3389/fmed.2020.569567/full>

Findings: Among 120 COVID-19 patients enrolled in the study, 74 were taking enoxaparin (4,000 or 6,000 units/day) and 46 fondaparinux (2.5 units/day). No statistically significant difference in demographic and laboratory and clinical characteristics between the two groups has been shown. During a median follow-up of 32 days, the cumulative incidence rates of VTE and bleeding events on pharmacological thromboprophylaxis with heparins were 19% and 8%, respectively. The incidence of both VTE (6.5 vs. 13.5%; $P = 0.36$) and bleeding events (6.5 vs. 4.1%; $P = 0.68$) did not show a significant difference between COVID-19 patients on fondaparinux compared with those on enoxaparin therapy. The regression model for the risk of outcome events according to different VTE prophylaxis drugs did not show significant differences. Although these results need confirmation by prospective studies including a larger population, our study provides preliminary evidence of a safe and efficacy use of fondaparinux for VTE prophylaxis in hospitalized COVID-19 patients.

38. **High-flow nasal cannula in COVID-19: Outcomes of application and examination of the ROX index to predict success.** Chandel A, Patolia S, Brown AW, et al. *Respir Care*. 2020 Dec 16:respcare.08631. doi: 10.4187/respcare.08631.

<http://rc.rcjournal.com/content/early/2020/12/16/respcare.08631>

Findings: 272 subjects with COVID-19 were managed with HFNC. 164 (60.3%) were successfully weaned from HFNC and 111 (67.7%) of those weaned were managed solely in non-ICU settings. ROX index >3.0 at 2, 6, and 12 hours after initiation of HFNC was 85.3% sensitive for identifying subsequent HFNC success. 108 subjects were intubated for failure of HFNC (61 early failures and 47 late failures). Mortality after HFNC failure was high (45.4%). There was no statistical difference in hospital mortality (39.3% vs. 53.2%; $P=0.18$) or any of the secondary endpoints between early and late HFNC failure groups. In this retrospective review, HFNC was a viable strategy and mechanical ventilation was avoided in the majority of subjects. In the minority that progressed to mechanical ventilation, duration of HFNC did not differentiate subjects with worse clinical outcomes. The ROX index was sensitive for the identification of subjects successfully weaned from HFNC. Prospective studies in COVID-19 are warranted to confirm these findings and to optimize patient selection for use of HFNC in this disease.

39. **Sofosbuvir and daclatasvir for the treatment of COVID-19 outpatients: a double-blind, randomized controlled trial.** Roozbeh F, Saeedi M, Alizadeh-Navaei R, et al. *J Antimicrob Chemother*. 2020 Dec 18:dkaa501. doi: 10.1093/jac/dkaa501.

<https://academic.oup.com/jac/advance-article/doi/10.1093/jac/dkaa501/6041772>

Findings: This was a randomized controlled clinical trial in outpatients with mild COVID-19. Patients were randomized into a treatment arm receiving sofosbuvir/daclatasvir plus

hydroxychloroquine or a control arm receiving hydroxychloroquine alone. The primary endpoint of the trial was symptom alleviation after 7 days of follow-up. The secondary endpoint of the trial was hospital admission. Between 8 April 2020 and 19 May 2020, 55 patients were recruited and allocated to either the sofosbuvir/daclatasvir treatment arm (n = 27) or the control arm (n = 28). There was no significant difference in symptoms at Day 7. In this study, sofosbuvir/daclatasvir did not significantly alleviate symptoms after 7 days of treatment compared with control. Although fewer hospitalizations were observed in the sofosbuvir/daclatasvir arm, this was not statistically significant. Sofosbuvir/daclatasvir significantly reduced the number of patients with fatigue and dyspnoea after 1 month. Larger, well-designed trials are warranted.

Transmission / Infection Control

40. Decontamination of N95 masks for re-use employing 7 widely available sterilization methods.

Kumar A, Kasloff SB, Leung A, et al. *PLoS One*. 2020 Dec 16;15(12):e0243965. doi: 10.1371/journal.pone.0243965. eCollection 2020.

<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0243965>

Findings: We sought to test the ability of 7 different decontamination methods: autoclave treatment, ethylene oxide gassing (ETO), low temperature hydrogen peroxide gas plasma (LT-HPGP) treatment, vaporous hydrogen peroxide (VHP) exposure, peracetic acid dry fogging (PAF), ultraviolet C irradiation (UVCI) and moist heat (MH) treatment to decontaminate a variety of different N95 masks following experimental contamination with SARS-CoV-2 or vesicular stomatitis virus as a surrogate. In addition, we sought to determine whether masks would tolerate repeated cycles of decontamination while maintaining structural and functional integrity. All methods except for UVCI were effective in total elimination of viable virus from treated masks. We found that all respirator masks tolerated at least one cycle of all treatment modalities without structural or functional deterioration as assessed by fit testing; filtration efficiency testing results were mostly similar except that a single cycle of LT-HPGP was associated with failures in 3 of 6 masks assessed. VHP, PAF, UVCI, and MH were associated with preserved mask integrity to a minimum of 10 cycles by both fit and filtration testing. A similar result was shown with ethylene oxide gassing to the maximum 3 cycles tested. Pleated, layered non-woven fabric N95 masks retained integrity in fit testing for at least 10 cycles of autoclaving but the molded N95 masks failed after 1 cycle; filtration testing however was intact to 5 cycles for all masks. The successful application of autoclaving for layered, pleated masks may be of particular use to institutions globally due to the virtually universal accessibility of autoclaves in health care settings. Given the ability to modify widely available heating cabinets on hospital wards in well-resourced settings, the application of moist heat may allow local processing of N95 masks.

41. Decontaminating N95 respirators during the Covid-19 pandemic: simple and practical approaches to increase decontamination capacity, speed, safety and ease of use.

Russo R, Levine C, Grady C, et al. *J Hosp Infect*. 2020 Dec 18:S0195-6701(20)30570-3. doi: 10.1016/j.jhin.2020.12.006.

<https://www.sciencedirect.com/science/article/pii/S0195670120305703?via%3Dihub>

Findings: We converted a decommissioned Biosafety Level 3 laboratory into a facility that could be used to decontaminate N95 respirators. N95 respirators were hung on metal racks, stacked in piles, placed in paper bags or covered with makeup or moisturizer. A VHP® VICTORY™ unit from STERIS was used to inject VHP into the facility. Biological and chemical indicators were used to validate the decontamination process. N95 respirators individually hung on metal racks were successfully decontaminated using VHP. N95 respirators were also successfully decontaminated when placed in closed paper bags or if stacked in piles of up to six. Stacking reduced the time needed to arrange N95 respirators for decontamination by approximately two-thirds while almost tripling facility capacity. Makeup and moisturizer creams did not interfere with the decontamination process. Respirator stacking can reduce the hands-on time and increase decontamination capacity. When personalization is needed, respirators can be decontaminated in labeled paper bags. Makeup or moisturizers do not appear to interfere with VHP decontamination.

42. **Face masks to prevent transmission of COVID-19: a systematic review and meta-analysis.** Li Y, Liang M, Gao L, et al. *Am J Infect Control*. 2020 Dec 18:S0196-6553(20)31043-9. doi: 10.1016/j.ajic.2020.12.007.

<https://www.sciencedirect.com/science/article/pii/S0196655320310439?via%3Dihub>

Findings: A total of 6 studies were included, involving 4 countries, after a total of 5,178 eligible articles were searched in databases and references. In general, wearing a mask was associated with a significantly reduced risk of COVID-19 infection. For the healthcare workers group, masks were shown to have a reduced risk of infection by nearly 70%. The results of this systematic review and meta-analysis support the conclusion that wearing a mask could reduce the risk of COVID-19 infection. Robust randomized trials are needed in the future to better provide evidence for these interventions.

43. **No Evidence of Re-infection or Person-to-Person Transmission in Cured COVID-19 Patients in Guangzhou, a Retrospective Observational Study.** Xu G, Liu F, Ye M, et al. *Front Med (Lausanne)*. 2020 Nov 30;7:593133. doi: 10.3389/fmed.2020.593133. eCollection 2020.

<https://www.frontiersin.org/articles/10.3389/fmed.2020.593133/full>

Findings: A total of 187 cured COVID-19 patients with antibody test were followed up every 2 weeks in this retrospective observational study. Assessment for general condition, symptoms, epidemiological contact history, PCR assay, and antibody tests were performed and recorded. There were 33 (17.6%) patients with negative results for IgG and 35 (18.7%) patients with positive results for IgM. The average days of antibody detection from disease onset were 53.0. PCR assay was positive in 10 (5.3%) patients during the follow-up. Neither IgG nor IgM results showed a relationship with PCR test results (all $P > 0.05$). Neither re-infection nor person-to-person transmission was found in the cured patients. Factors associated with appearance of antibody comprised hospitalization days (OR: 1.06, 95%CI: 1.02-1.11, $P = 0.006$) and antibiotics treatment (OR: 3.50, 95%CI: 1.40-8.77, $P = 0.007$). Conclusions: In our study, no evidence of person-to-person transmission was found in cured COVID-19 patients. There seemed to be no re-infection in the cured COVID-19 patients in Guangzhou. These findings suggest that the cured do not cause the spread of disease. Additionally, neither IgG nor IgM can be used to replace the PCR test in cured patients.

Vaccine

44. **Reserving coronavirus disease 2019 vaccines for global access: cross sectional analysis.** So AD, Woo J. *BMJ* 2020 Dec 15. <https://doi.org/10.1136/bmj.m4750>
Findings: As of 15 November 2020, several countries have made premarket purchase commitments totaling 7.48 billion doses, or 3.76 billion courses, of covid-19 vaccines from 13 vaccine manufacturers. Just over half (51%) of these doses will go to high income countries, which represent 14% of the world's population. The US has reserved 800 million doses but accounts for a fifth of all covid-19 cases globally (11.02 million cases), whereas Japan, Australia, and Canada have collectively reserved more than one billion doses but do not account for even 1% of current global covid-19 cases globally (0.45 million cases). If these vaccine candidates were all successfully scaled, the total projected manufacturing capacity would be 5.96 billion courses by the end of 2021. Up to 40% (or 2.34 billion) of vaccine courses from these manufacturers might potentially remain for low and middle income countries—less if high income countries exercise scale-up options and more if high income countries share what they have procured. Prices for these vaccines vary by more than 10-fold, from \$6.00 (£4.50; €4.90) per course to as high as \$74 per course. With broad country participation apart from the US and Russia, the COVAX Facility—the vaccines pillar of the World Health Organization's Access to COVID-19 Tools (ACT) Accelerator—has secured at least 500 million doses, or 250 million courses, and financing for half of the targeted two billion doses by the end of 2021 in efforts to support globally coordinated access to covid-19 vaccines. This study provides an overview of how high income countries have secured future supplies of covid-19 vaccines but that access for the rest of the world is uncertain. Governments and manufacturers might provide much needed assurances for equitable allocation of covid-19 vaccines through greater transparency and accountability over these arrangements.
**See also: [Global, regional, and national estimates of target population sizes for covid-19 vaccination: descriptive study](#). Wang W, Wu Q, Yang J, Dong K, Chen X, Bai X, Chen X, Chen Z, Viboud C, Ajelli M, Yu H. *BMJ* 2020 Dec 15. doi: <https://doi.org/10.1136/bmj.m4704>; [Equitable global access to coronavirus disease 2019 vaccines](#). Schwartz JL. *BMJ* 2020 Dec 15. <https://doi.org/10.1136/bmj.m4735>
45. **A single dose of recombinant VSV-ΔG-spike vaccine provides protection against SARS-CoV-2 challenge.** Yahalom-Ronen Y, Tamir H, Melamed S, et al. *Nat Commun.* 2020 Dec 16;11(1):6402. doi: 10.1038/s41467-020-20228-7. <https://www.nature.com/articles/s41467-020-20228-7>
Findings: Here, we show the development of a replication competent recombinant VSV-ΔG-spike vaccine, in which the glycoprotein of VSV is replaced by the spike protein of SARS-CoV-2. In-vitro characterization of this vaccine indicates the expression and presentation of the spike protein on the viral membrane with antigenic similarity to SARS-CoV-2. A golden Syrian hamster in-vivo model for COVID-19 is implemented. We show that a single-dose vaccination results in a rapid and potent induction of SARS-CoV-2 neutralizing antibodies. Importantly, vaccination protects hamsters against SARS-CoV-2 challenge, as demonstrated by the abrogation of body weight loss, and alleviation of the extensive tissue damage and viral loads in lungs and nasal

turbinates. Taken together, we suggest the recombinant VSV-ΔG-spike as a safe, efficacious and protective vaccine against SARS-CoV-2.

- 46. T cell and antibody responses induced by a single dose of ChAdOx1 nCoV-19 (AZD1222) vaccine in a phase 1/2 clinical trial.** Oxford COVID Vaccine Trial Group. *Nat Med.* 2020 Dec 17. doi: 10.1038/s41591-020-01194-5. <https://www.nature.com/articles/s41591-020-01194-5>
Findings: ChAdOx1 nCoV-19 (AZD1222) is a candidate SARS-CoV-2 vaccine comprising a replication-deficient simian adenovirus expressing full-length SARS-CoV-2 spike protein. We recently reported preliminary safety and immunogenicity data from a phase 1/2 trial of the ChAdOx1 nCoV-19 vaccine (NCT04400838)⁷ given as either a one- or two-dose regimen. The vaccine was tolerated, with induction of neutralizing antibodies and antigen-specific T cells against the SARS-CoV-2 spike protein. Here we describe, in detail, exploratory analyses of the immune responses in adults, aged 18-55 years, up to 8 weeks after vaccination with a single dose of ChAdOx1 nCoV-19 in this trial, demonstrating an induction of a Th1-biased response characterized by interferon- γ and tumor necrosis factor- α cytokine secretion by CD4+ T cells and antibody production predominantly of IgG1 and IgG3 subclasses. CD8+ T cells, of monofunctional, polyfunctional and cytotoxic phenotypes, were also induced. Taken together, these results suggest a favorable immune profile induced by ChAdOx1 nCoV-19 vaccine, supporting the progression of this vaccine candidate to ongoing phase 2/3 trials to assess vaccine efficacy.
- 47. Phase 1/2 trial of SARS-CoV-2 vaccine ChAdOx1 nCoV-19 with a booster dose induces multifunctional antibody responses.** Oxford COVID Vaccine Trial Group. *Nat Med.* 2020 Dec 17. doi: 10.1038/s41591-020-01179-4. <https://www.nature.com/articles/s41591-020-01179-4>
Findings: Previously, we reported early immunogenicity and safety outcomes of a viral vector coronavirus vaccine, ChAdOx1 nCoV-19 (AZD1222), in a single-blinded phase 1/2 randomized controlled trial of healthy adults aged 18-55 years. Now we describe safety and exploratory humoral and cellular immunogenicity of the vaccine, from subgroups of volunteers in that trial, who were subsequently allocated to receive a homologous full-dose (SD/SD D56; n = 20) or half-dose (SD/LD D56; n = 32) ChAdOx1 booster vaccine 56 d following prime vaccination. Previously reported immunogenicity data from the open-label 28-d interval prime-boost group (SD/SD D28; n = 10) are also presented to facilitate comparison. Additionally, we describe volunteers boosted with the comparator vaccine (MenACWY; n = 10). In this interim report, we demonstrate that a booster dose of ChAdOx1 nCoV-19 is safe and better tolerated than priming doses. Using a systems serology approach we also demonstrate that anti-spike neutralizing antibody titers, as well as Fc-mediated functional antibody responses, including antibody-dependent neutrophil/monocyte phagocytosis, complement activation and natural killer cell activation, are substantially enhanced by a booster dose of vaccine. A booster dose of vaccine induced stronger antibody responses than a dose-sparing half-dose boost, although the magnitude of T cell responses did not increase with either boost dose. These data support the two-dose vaccine regime that is now being evaluated in phase 3 clinical trials.

Whole Person Care

48. **PREVALENCE OF MALNUTRITION IN COVID-19 INPATIENTS: THE NUTRICOV STUDY.** Rouget A, Vardon-Bounes F, Lorber P, et al. *Br J Nutr.* 2020 Dec 21:1-24. doi: 10.1017/S0007114520005127. <https://www.cambridge.org/core/journals/british-journal-of-nutrition/article/prevalence-of-malnutrition-in-covid19-inpatients-the-nutricov-study/2816476F3935201368113E13203298A5>
Findings: 80 patients were prospectively enrolled in the study. Thirty patients (37.5%) had criteria for malnutrition. The need for ICU admission was similar in the two groups. Three patients who died (3.75%) were malnourished. Multivariate analysis exhibited that low BMI, dyslipidemia, oral intakes reduction <50% and GFR at admission were associated with the occurrence of malnutrition in COVID-19 inpatients. We demonstrate the existence of a high prevalence of malnutrition (37.5%) in a general cohort of COVID-19 inpatients according to GLIM criteria. Considering this high prevalence, nutritional support in COVID-19 care seems an essential element.

Women & Children

49. **Epidemiology of COVID-19 infection in young children under five years: A systematic review and meta-analysis.** Bhuiyan MU, Stiboy E, Hassan MZ, et al. *Vaccine.* 2020 Dec 5:S0264-410X(20)31570-X. doi: 10.1016/j.vaccine.2020.11.078. <https://www.sciencedirect.com/science/article/pii/S0264410X2031570X?via%3Dihub>
Findings: We identified 1,964 articles, of which, 65 articles were eligible for systematic review that represented 1,214 children younger than five years with laboratory-confirmed COVID-19 infection. The pooled estimates showed that 50% young COVID-19 cases were infants; 53% were male; 43% were asymptomatic and 7% had severe disease that required intensive-care-unit admission. Of 139 newborns from COVID-19 infected mothers, five (3.6%) were COVID-19 positive. There was only one death recorded. This systematic review reports the largest number of children younger than five years with COVID-19 infection till date. Our meta-analysis shows nearly half of young COVID-19 cases were asymptomatic and half were infants, highlighting the need for ongoing surveillance to better understand the epidemiology, clinical pattern, and transmission of COVID-19 to develop effective preventive strategies against COVID-19 disease in young paediatric population.
50. **Factors Associated with Severe SARS-CoV-2 Infection.** Ouldali N, Yang DD, Madhi F, et al. *Pediatrics.* 2020 Dec 15:e2020023432. doi: 10.1542/peds.2020-023432. <https://pediatrics.aappublications.org/content/pediatrics/early/2020/12/11/peds.2020-023432.full.pdf>
Findings: 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.

51. Pediatric Ischemic Stroke: An Infrequent Complication of SARS-CoV-2. International Pediatric Stroke Study Group. *Ann Neurol.* 2020 Dec 17. doi: 10.1002/ana.25991.

<https://onlinelibrary.wiley.com/doi/10.1002/ana.25991>

Findings: Of 42 centers with SAR-CoV-2 hospitalization numbers, 8/971 (0.82%) with SARS-CoV-2 had ischemic strokes. Proportions of stroke cases positive for SARS-CoV-2 from March-May 2020 were: 1/108 neonatal AIS (0.9%), 0/33 neonatal cerebral sinovenous thrombosis (CSVT; 0%), 6/166 childhood AIS (3.6%), and 1/54 childhood CSVT (1.9%) cases. However, only 30.5% of neonates and 60% of children with strokes were tested for SARS-CoV-2. Therefore, these proportions represent 2.9%, 0%, 6.1%, and 3.0% of stroke cases tested for SARS-CoV-2. Seven of eight with SARS-CoV-2 had additional established stroke risk factors. As in adults, pediatric stroke is an infrequent complication of SARS-CoV-2, and SARS-CoV-2 was detected in only 4.7% of pediatric ischemic stroke patients tested. However, $<50\%$ of strokes were tested. SARS-CoV-2 testing should be considered in pediatric stroke patients as the pandemic continues to determine SARS-CoV-2's role in pediatric stroke.

52. Systematic review of reviews of symptoms and signs of COVID-19 in children and adolescents.

Viner RM, Ward JL, Hudson LD, et al. *Arch Dis Child.* 2020 Dec 17:archdischild-2020-320972. doi: 10.1136/archdischild-2020-320972.

<https://adc.bmj.com/content/early/2020/12/16/archdischild-2020-320972.long>

Findings: 1325 studies were identified and 18 reviews were included. Eight were high quality, 7 medium and 3 low quality. All reviews were dominated by studies of hospitalised children. The proportion of asymptomatic CYP ranged from 14.6% to 42%. Fever and cough were the the most common symptoms; proportions with fever ranged from 46% to 64.2% and with cough from 32% to 55.9%. All other symptoms or signs including rhinorrhoea, sore throat, headache, fatigue/myalgia and gastrointestinal symptoms including diarrhoea and vomiting were infrequent, occurring in less than 10%-20%. Fever and cough are the most common symptoms in CYP with COVID-19, with other symptoms infrequent. Further research on symptoms in community samples are needed to inform pragmatic identification and testing programmes for CYP.

GUIDELINES & CONSENSUS STATEMENTS

[Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance.](#) *Lancet Infect Dis.* 2020 Dec 14:S1473-3099(20)30847-1. doi: 10.1016/S1473-3099(20)30847-1.

[The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine - United States, December 2020.](#) *MMWR Morb Mortal Wkly Rep.* 2020 Dec 18;69(50):1922-1924. doi: 10.15585/mmwr.mm6950e2.

FDA / CDC / NIH / WHO Updates

CDC - [Interim Clinical Considerations for Use of Pfizer-BioNTech COVID-19 Vaccine](#)

CDC - [COVID-19 Vaccines and Severe Allergic Reactions](#)

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

FDA briefing on Moderna vaccine: [Vaccines and Related Biological Products Advisory Committee Meeting December 17, 2020](#)

FDA - [issues emergency use authorization for the Moderna COVID-19 Vaccine](#), Dec 18 2020.

Commentary & News

[COVID-19 as the Leading Cause of Death in the United States.](#) Woolf SH, Chapman DA, Lee JH. *JAMA.* 2020 Dec 17. doi: 10.1001/jama.2020.24865.

[FDA investigating allergic reactions to Pfizer vaccine reported in multiple states](#)

New York Times - [The Coronavirus Is Mutating. What Does That Mean for Us?](#)

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