New Research

*note, PREPRINTS have not undergone formal peer review

COVID-19 related publications by Providence caregivers – see Digital Commons

Basic Science / Virology / Pre-clinical


   Findings: Using a panel of 37 convalescent COVID-19 human serum samples, we showed that the magnitude and specificity of responses varied across individuals, independent of their reactivity to seasonal human coronaviruses (HCoVs). These data suggest that COVID-19 vaccines will elicit primary humoral immune responses in naïve individuals and variable responses in those previously exposed to SARS-CoV-2. Unlike the limited cross-coronavirus reactivities in humans, serum samples from 96 dogs and 10 cats showed SARS-CoV-2 protein-specific responses focused on non-S1 proteins. The correlation of this response with those to other coronaviruses suggests that the antibodies are cross-reactive and generated to endemic viruses within these hosts, which must be considered in seroepidemiologic studies. We conclude that substantial variation in antibody generation against coronavirus proteins will influence interpretations of serologic data in the clinical and veterinary settings.

Clinical Syndrome


   Findings: A total of 817 older patients with COVID-19 were included, of whom 386 (47%) were male, 493 (62%) were White, 215 (27%) were Black, and 54 (7%) were Hispanic or Latinx. The mean age of patients was 77.7 (8.2) years. Of included patients, 226 (28%) had delirium at presentation, and delirium was the sixth most common of all presenting symptoms and signs. Among the patients with delirium, 37 (16%) had delirium as a primary symptom and 84 (37%) had no typical COVID-19 symptoms or signs, such as fever or shortness of breath. Factors associated with delirium were age older than 75 years, living in a nursing home or assisted living, prior use of psychoactive medication, vision impairment, hearing impairment, stroke, and Parkinson disease. Delirium was associated with intensive care unit stay and death. These
findings suggest the clinical importance of including delirium on checklists of presenting signs and symptoms of COVID-19 that guide screening, testing, and evaluation.


Findings: We identified 1162 studies, of which 83 studies (n=27492, 61.4% female) were included in the meta-analysis. Overall, the pooled prevalence of olfactory dysfunction in COVID-19 patients was 47.85%. Anosmia, hyposmia, and dysosmia were observed in 35.39%, 36.15%, and 2.53% of the patients, respectively. The prevalence of olfactory dysfunction in COVID-19 patients was found to be 47.85% based on high quality evidence. Due to the subjective measures of most studies pooled in the analysis, further studies with objective measures are advocated to confirm the finding.


Findings: We identified 40 SP in 71,904 patients with COVID-19 attending EDs. This relative frequency was higher than that of non-COVID patients. Compared with COVID patients without SP, COVID patients developing SP more frequently had dyspnea and chest pain, low pulsioxymetry, tachypnea and increased leukocyte count. SP as a form of COVID presentation at the ED is unusual (<1‰ cases) but is more frequent than in the non-COVID population and could be associated with worse outcomes than SP in non-COVID patients and COVID patients without SP.

**Diagnostics & Screening**


Findings: To compare sensitivity of specimens for COVID-19 diagnosis, we tested 151 nasopharyngeal/mid-turbinate swab pairs from 117 COVID-19 inpatients using RT-PCR. Sensitivity was 94% for nasopharyngeal and 75% for mid-turbinate swabs (p=0.0001). In 88 nasopharyngeal/mid-turbinate pairs with matched saliva, sensitivity was 86% for nasopharyngeal swabs and 88% for combined mid-turbinate swabs/saliva.

Findings: Although these tests give an indication about the general health status of patients and some tests may be specific indicators for inflammatory processes, none of the tests we investigated are useful for accurately ruling in or ruling out COVID-19 on their own. Studies were done in specific hospitalized populations, and future studies should consider non-hospital settings to evaluate how these tests would perform in people with milder symptoms.

Findings: For the assays that were evaluated, the sensitivity and specificity for any reactive band ranged from 55%-97% and 78%-100%, respectively. When assessing the performance of the IgM and the IgG bands alone, sensitivity and specificity ranged from 0%-88% and 80%-100% for IgM and 25%-95% and 90%-100% for IgG. Longitudinal testing revealed that median time post symptom onset to a positive result was 7 days for IgM and 8.2 days for IgG. The testing performance varied widely among LFAs with most variation related to the sensitivity of the assays. The IgM band was most likely to misclassify pre-pandemic samples. The appearance of IgM and IgG bands occurred almost simultaneously.

Findings: We enrolled a total of 626 participants (71% of the community population) for PCR- and antibody testing in the study. All actual SARS-CoV-2 PCR tests were negative. Fifty-two out of 620 (8.4%) participants had antibodies against SARS-CoV-2 in at least two different assays. There were 38 participants with previously PCR-confirmed SARS-CoV-2 infection. Of those, only 19 (50%) displayed anti-SARS-CoV-2 antibodies. We also show that antibody positive participants with symptoms compatible with a respiratory tract infection had significantly higher antibody levels than asymptomatic participants. Persisting viral replication was not detected. Our data question the relevance and reliability of IgG antibody testing to detect past SARS-CoV-2 infections six weeks after an outbreak. We conclude that assessing immunity for SARS-CoV-2 infection should not only rely on antibody tests.

Epidemiology & Public Health

https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2773576?resultClick=1
Findings: This repeated, cross-sectional study conducted across all 50 states, the District of Columbia, and Puerto Rico used a convenience sample of residual serum specimens provided by persons of all ages that were originally submitted for routine screening or clinical management from 2 private clinical commercial laboratories. Samples were obtained during 4 collection periods: July 27 to August 13, August 10 to August 27, August 24 to September 10, and September 7 to September 24, 2020. Of 177 919 serum samples tested, 103 771 (58.3%) were from women, 26 716 (15.0%) from persons 17 years or younger, 47 513 (26.7%) from persons 65 years or older, and 26 290 (14.8%) from individuals living in nonmetropolitan areas. Jurisdiction-level seroprevalence over 4 collection periods ranged from less than 1% to 23%. In 42 of 49 jurisdictions with sufficient samples to estimate seroprevalence across all periods, fewer than 10% of people had detectable SARS-CoV-2 antibodies. Seroprevalence estimates varied between sexes, across age groups, and between metropolitan/nonmetropolitan areas. Changes from period 1 to 4 were less than 7 percentage points in all jurisdictions and varied across sites. This cross-sectional study found that as of September 2020, most persons in the US did not have serologic evidence of previous SARS-CoV-2 infection, although prevalence varied widely by jurisdiction. Biweekly nationwide testing of commercial clinical laboratory sera can play an important role in helping track the spread of SARS-CoV-2 in the US.

Healthcare Delivery & Healthcare Workers


FINDINGS: Forty-nine studies, including 127,480 HCWs met the inclusion criteria. The estimated overall seroprevalence of SARS-CoV-2 antibodies among HCWs was 8.7%. Seroprevalence was higher in studies that were conducted in North America (12.7%) compared to those in Europe (8.5%), Africa (8.2), and Asia (4%). The following factors were associated with seropositivity: male gender, Black, Asian, and Hispanic HCWs, work in a COVID-19 unit, patient-related work, frontline health care workers, health care assistants, personal protective equipment shortage, self-reported belief for previous SARS-CoV-2 infection, previous positive polymerase chain reaction test, and household contact with suspected or confirmed COVID-19 patients. The seroprevalence of SARS-CoV-2 antibodies among HCWs is high. Excellent adherence to infection prevention and control measures, sufficient and adequate personal protective equipment, and early recognition, identification and isolation of HCWs that are infected with SARS-CoV-2 are imperative to decrease the risk of SARS-CoV-2 infection.

Laboratory Results

Findings: The ABO and rhesus (Rh) blood groups may influence risk for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. A total of 225,556 persons were included, with a mean age of 54 years. The aRR of SARS-CoV-2 infection for O blood group versus A, AB, and B blood groups together was 0.88. Rhesus-negative (Rh-) blood type was protective against SARS-CoV-2 infection, especially for those who were O-negative. There was also a lower risk for severe COVID-19 illness or death associated with type O blood group versus all others. The O and Rh- blood groups may be associated with a slightly lower risk for SARS-CoV-2 infection and severe COVID-19 illness.

Prognosis

Findings: Three days after ICU admission, 164 patients were present in ICU and included in the analysis. One-hundred and twenty-one patients (74%) were tracheostomized, whereas the other 43 (26%) were managed with translaryngeal intubation only. Early percutaneous tracheostomy was associated with lower hospital mortality. Sixty-six of tracheostomized patients (55%) were discharged alive from the hospital. Age and male sex were the only characteristics that were independently associated with mortality in the tracheostomized patients (45.5% and 62.8% in tracheostomized and nontracheostomized patients, respectively; p = 0.009). Tracheostomy tube was removed in 47 of the tracheostomized patients (71%). The only variable independently associated with weaning from tracheostomy at ICU discharge was a faster start of spontaneous breathing after tracheotomy was performed. Early percutaneous tracheostomy was safe and effective in coronavirus disease 2019 patients, giving a good chance of survival and of weaning from tracheostomy cannula at ICU discharge.

Findings: We identified 88,747 patients tested for SARS-CoV-2 between 3/1/20-5/14/20 in the VA national healthcare system, including 75,315 with no cirrhosis-SARS-CoV-2 negative (C0-S0), 9826 with no cirrhosis-SARS-CoV-2 positive (C0-S1); 3301 with cirrhosis-SARS-CoV-2 negative (C1-S0); and 305 with cirrhosis-SARS-CoV-2 positive (C1-S1). Patients were followed through 6/22/20. SARS-CoV-2 infection was associated with a 3.5-fold increase in mortality in patients with cirrhosis. Cirrhosis was associated with a 1.7-fold increase in mortality in patients with SARS-CoV-2 infection.


Findings: Among 7,868 patients hospitalized with COVID-19, 33.0% were Hispanic, 25.5% were non-Hispanic Black, 6.3% were Asian, and 35.2% were non-Hispanic White. Hispanic and Black patients were younger than non-Hispanic White and Asian patients and were more likely to be uninsured. Black patients had the highest prevalence of obesity, hypertension, and diabetes. Black patients also had the highest rates of mechanical ventilation (23.2%) and renal replacement therapy (6.6%) but the lowest rates of remdesivir use (6.1%). Overall mortality was 18.4% with 53% of all deaths occurring in Black and Hispanic patients. The adjusted odds ratios (ORs) for mortality were 0.93 (95% confidence interval [CI] 0.76-1.14) for Black patients, 0.90 (95% CI 0.73-1.11) for Hispanic patients, and 1.31 (95% CI 0.96-1.80) for Asian patients compared with non-Hispanic White patients. The median OR across hospitals was 1.99 (95% CI 1.74-2.48). Results were similar for MACE. Asian patients had the highest COVID-19 cardiorespiratory severity at presentation (adjusted OR 1.48, 95% CI 1.16-1.90). Although in-hospital mortality and MACE did not differ by race/ethnicity after adjustment, Black and Hispanic patients bore a greater burden of mortality and morbidity due to their disproportionate representation among COVID-19 hospitalizations.


Findings: Obese patients are more likely to be hospitalized with COVID-19 and are at higher risk of in-hospital death or mechanical ventilation particularly if young (age ≤50 years). Obese patients are also at higher risk for venous thromboembolism and dialysis. These observations support clear public health messaging and rigorous adherence to COVID-19 prevention strategies in all obese individuals regardless of age.


Findings: Thirteen studies involving 1579 patients reported the predictive value of NLR on disease severity. NLR has good predictive values on disease severity and mortality in patients with COVID-19 infection. Evaluating NLR can help clinicians identify potentially severe cases early, conduct early triage and initiate effective management in time, which may reduce the overall mortality of COVID-19.

Findings: We retrospectively collected all the cases of coronavirus disease 2019 acute respiratory distress syndrome patients (n = 46) admitted to our 34-bed ICU between March 24, 2020, and May 25, 2020, and identified six patients that met the diagnosis of invasive pulmonary aspergillosis according to previously established definitions. This population exhibited higher severity scores at admission and less hospital discharge compared with noninvasive pulmonary aspergillosis patients. Chronic obstructive pulmonary disease, malnutrition, and systemic corticosteroid use were identified as risk factors for invasive pulmonary aspergillosis in coronavirus disease 2019-induced acute respiratory distress syndrome patients. Coronavirus disease 2019-associated pulmonary aspergillosis may be a serious concern regarding corticosteroids use to control the inflammatory response of coronavirus disease 2019-induced acute respiratory distress syndrome.


Findings: Patients with hypertension, heart failure, diabetes, kidney disease, or ischemic heart disease registered in the Swedish National Patient Registry until February 1st 2020 were included and followed until May 31st 2020. Multivariable logistic and Cox regressions were fitted to investigate the association between ACEi/ARB and MRA and risk of hospitalization/death for Covid-19 in the overall population, and of all-cause mortality in Covid-19 cases. Of 1,387,746 patients (60% receiving ACEi/ARB and 5.8% MRA) 7,146 (0.51%) had incident hospitalization/death from Covid-19. After adjustment for 45 variables, ACEi/ARB use was associated with a reduced risk of hospitalization/death for Covid-19. In a 1.4 million nation-wide cohort, use of RAASi was not associated with increased risk of hospitalization for or death from Covid-19.


Findings: A total of 375 hospitalized patients were included. There were 128 sBSIs during the hospitalization. For the first set of positive blood cultures, 117 (91.4%) were bacterial and 7 (5.5%) were fungal. Those with sBSI were more likely to have altered mental status, lower mean percent oxygen saturation on room air, have septic shock and be admitted to the intensive care unit compared to the controls. In-hospital mortality was higher in those with a sBSI versus controls (53.1% vs 32.8%). We observed hospitalized adult patients with severe COVID-19 and sBSI had a more severe initial presentation, prolonged hospital course, and worse clinical outcomes. To maintain antimicrobial stewardship principles, further prospective studies are necessary to better characterize risk factors and prediction modeling to better understand when to suspect and empirically treat for sBSI in severe COVID-19.

**Findings:** Acute ischemic stroke and large vessel occlusion can be concurrent with COVID-19 infection. Outcomes after mechanical thrombectomy (MT) for large vessel occlusion in patients with COVID-19 are substantially unknown. Our aim was to study early outcomes after MT in patients with COVID-19. Multicenter, European, cohort study involving 34 stroke centers in France, Italy, Spain, and Belgium. We evaluated 93 patients with COVID-19 with large vessel occlusion who underwent MT (median age, 71 years [interquartile range, 59-79]; 63 men [67.7%]). The 29% rate of 30-day mortality after MT among patients with COVID-19 is not negligible. Abnormalities of lymphocyte count, LDH and aspartate may depict a patient's profiles with poorer outcomes after MT.

**Survivorship & Rehabilitation**


**Findings:** 124 patients (age 59±14 years, 60% male) were included; 27 with mild, 51 with moderate, 26 with severe and 20 with critical disease. Lung diffusion capacity was below lower limit of normal in 42% of discharged patients. Ninety-nine percent of discharged patients had reduced ground-glass opacification on repeat CT imaging, and normal chest X-rays were found in 93% of patients with mild diseases. Residual pulmonary parenchymal abnormalities were present in 91% of discharged patients and correlated with reduced lung diffusion capacity. Twenty-two percent had low exercise capacity, 19% low fat-free mass index, and problems in mental and/or cognitive function were found in 36% of the patients. Health status was generally poor, particularly in the domains: functional impairment (64%), fatigue (69%) and QoL (72%). This comprehensive health assessment revealed severe problems in several health domains in a substantial number of ex-COVID-19 patients. Longer follow-up studies are warranted to elucidate natural trajectories and to find predictors of complicated long-term trajectories of recovery.


**Findings:** At the time of the positive retest, we were able to acquire a complete genome sequence from patient 1, a 21-year-old previously healthy woman. In this patient, through the phylogenetic analysis, we confirmed that the viral RNA of positive retest was clustered into a subgroup distinct from that of the initial infection, suggesting that there was a reinfection of SARS-CoV-2 with a subtype that was different from that of the primary strain. Reinfection with a genetically distinct SARS-CoV-2 strain may occur in an immunocompetent patient shortly after
recovery from mild COVID-19. SARS-CoV-2 infection may not confer immunity against a
different SARS-CoV-2 strain.

23. Surviving COVID-19 after Hospital Discharge: Symptom, Functional, and Adverse Outcomes of
Findings: 1409 patients with COVID-19 admitted to home health care (HHC) between 1 April
and 15 June 2020 after hospitalization. After an average of 32 days in HHC, 94% of patients
were discharged and most achieved statistically significant improvements in symptoms and
function. Symptom burden and functional dependence were common at the time of HHC
admission but improved for most patients. Comorbid conditions of heart failure and diabetes,
as well as characteristics present at admission, identified patients at greatest risk for an adverse
event.

Therapeutics

https://academic.oup.com/ofid/article/7/11/ofaa481/5922322
Findings: One hundred thirteen patients requiring mechanical ventilation were observed for a
median of 31 days of follow-up; 32% died, 69% were extubated, and 66% were discharged alive
from the hospital. Among 33 treated with remdesivir (RDV), lower mortality (15.2% vs 38.8%)
and higher rates of extubation (88% vs 60%), ventilator-free days, and hospital discharge (85%
vs 59%) were observed. In our cohort of mechanically ventilated patients, RDV was not
associated with a significant reduction of mortality, but it was consistently associated with
shorter duration of mechanical ventilation and higher probability of hospital discharge,
independent of other risk factors.

25. Efficacy and Safety of Favipiravir, an Oral RNA-Dependent RNA Polymerase Inhibitor, in Mild-
to-Moderate COVID-19: A Randomized, Comparative, Open-Label, Multicenter, Phase 3
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7668212/
Findings: From May 14-July 3, 2020, 150 patients were randomized to favipiravir (n = 75) or
control (n = 75). Median time to cessation of viral shedding was 5 days versus 7 days, and
median time to clinical cure was 3 days versus 5 days, for favipiravir and control, respectively.
Adverse events were observed in 36% of favipiravir and 8% of control patients. One control
patient died due to worsening disease. Lack of statistical significance on the primary endpoint
was confounded by limitations of the RT-PCR assay. Significant improvement in time to clinical
cure suggests favipiravir may be beneficial in mild-to-moderate COVID-19.

Findings: We conducted a single-arm phase 2 trial of low-dose tocilizumab in non-intubated hospitalized adult patients with COVID-19, radiographic pulmonary infiltrate, fever, and C-reactive protein (CRP) ≥ 40 mg/L. We hypothesized that doses significantly lower than the emerging standards of 400 mg or 8 mg/kg would resolve clinical and laboratory indicators of hyperinflammation. A dose range from 40 to 200 mg was evaluated, with allowance for one repeat dose at 24 to 48 hours. The primary objective was to assess the relationship of dose to fever resolution and CRP response. Thirty-two patients received low-dose tocilizumab, with the majority experiencing fever resolution (75%) and CRP decline consistent with IL-6 pathway abrogation (86%) in the 24-48 hours following drug administration. There was no evidence of a relationship between dose and fever resolution or CRP decline over the dose range of 40-200 mg. Within the 28-day follow-up, 5 (16%) patients died. For patients who recovered, median time to clinical recovery was 3 days (IQR, 2-5). Clinically presumed and/or cultured bacterial superinfections were reported in 5 (16%) patients. Low-dose tocilizumab was associated with rapid improvement in clinical and laboratory measures of hyperinflammation in hospitalized patients with COVID-19. Results of this trial provide rationale for a randomized, controlled trial of low-dose tocilizumab in COVID-19.


Findings: We retrospectively assessed the effectiveness and safety of NIPPV in a cohort of COVID-19 patients consecutively admitted to the COVID-19 general wards of a medium-size Italian hospital, from March 6 to May 7, 2020. HCWs caring for COVID-19 patients were monitored, undergoing nasopharyngeal swab for SARS-CoV-2 in case of onset of COVID-19 symptoms, and periodic SARS-CoV-2 screening serology. Overall, 50 patients received NIPPV, of which 22 (44%) were successfully weaned, avoiding endotracheal intubation and AHFR-related death. Due to limited life expectancy, 25 (50%) of 50 NIPPV-treated patients received a DNI order. Among these, only 6 (24%) were weaned from NIPPV. Of the remaining 25 NIPPV-treated patients without treatment limitations, 16 (64%) were successfully weaned, 9 (36%) underwent delayed ETI and, of these, 3 (33.3%) died. NIPPV success was predicted by the use of corticosteroids and the increase in the PaO2/FiO2 ratio measured 24-48 h after NIPPV initiation. During the study period, 2 of 124 (1.6%) HCWs caring for COVID-19 patients were diagnosed with SARS-CoV-2 infection. Apart from patients with limited life expectancy, NIPPV was effective in a substantially high percentage of patients with COVID-19-associated AHFR. The risk of SARS-CoV-2 infection among HCWs was low.


Findings: 143 patients underwent tracheostomy, 58 (41%) via a ST, and 85 (59%) via a PT. There were no significant differences in patient characteristics between the two groups, except that
more patients who had a history of ECMO underwent PT (11% vs 2%). The rapid formation of a multi-disciplinary team allows for the efficient evaluation and performance of a large volume of tracheostomies in a resource-limited setting. Bedside tracheostomy in COVID-19 does not cause additional harm to patients if performed after 2 weeks from intubation. It also appears to be safe for proceduralists to perform in this timeframe. The manner of tracheostomy does not change outcomes significantly if it is performed safely and efficiently.


Findings: Twenty-one patients received hydroxychloroquine with lopinavir/ritonavir (median age 68 years; 10 males) and 25 received hydroxychloroquine with darunavir/ritonavir (median age 71 years; 15 males). During treatment, eight patients (17.4%) developed ECG abnormalities. Ten patients discontinued treatment, including seven for ECG abnormalities a median of 5 days after starting treatment. All ECG abnormalities reversed 1-2 days after interrupting treatment. Four patients died within 14 days. ECG abnormalities were significantly associated with age over 70 years, coexisting conditions and initial potential drug interactions, but not with the hydroxychloroquine concentration. Of the patients with COVID-19 who received hydroxychloroquine with lopinavir or darunavir, 17% had ECG abnormalities, mainly related to age or in those with a history of cardiovascular disease.


Findings: 120 COVID-19 patients with hyperinflammation (median age 62 years, 80.0% males) were evaluated. Of these, 65 were treated with anakinra and methylprednisolone and 55 were untreated historical controls. At 28 days, mortality was 13.9% in treated patients and 35.6% in controls. Unadjusted and adjusted risk of death was significantly lower for treated patients compared to controls. No significant differences in bloodstream infections or laboratory alterations were registered. Treatment with anakinra plus methylprednisolone may be a valid therapeutic option in COVID-19 patients with hyperinflammation and respiratory failure, also on mechanical ventilation. Randomized, controlled trials including use of either agent alone are needed to confirm these results.


Findings: Of the 516 patients in this study, 104 (20.1%) received IL6i. The estimate of the average treatment effect adjusted for confounders suggested a 37% reduction in the odds of in-hospital mortality in those who received IL-6i, compared with those who did not. Despite low
precision, our findings suggested a relatively large effect size of IL6i in reducing the odds of COVID-19 related in-hospital mortality.


In SARS-CoV-2 infection, the viral load peaks early setting off a cascade of immune dysregulation that persists well after viral clearance. Severe COVID-19 is marked by aberrant innate and adaptive immune responses with an abnormal cytokine profile and a prolonged illness course with multisystem organ dysfunction. Antiviral treatments have yet to show benefit later in critical illness. Taken together, this raises the concern that a purely antiviral treatment approach may be insufficient. A number of immunomodulatory strategies are being tested, including corticosteroids, cytokine and anti-cytokine therapies, small molecule inhibitors, and cellular therapeutics. The only drug to date to show a mortality benefit for COVID-19 in a randomized control trial is dexamethasone, but there remains uncertainty about which patients may benefit most and longer-term complications including secondary infections. Here we review the immune dysregulation of severe COVID-19, the existing data behind various immunomodulatory strategies, and consider future directions of study.


Findings: The mean time from admission to IVIg initiation was 3.84 ± 3.35 days. The length of hospital stay was significantly lower for the control group than that of the intervention group. There was a significant positive relationship between the time from hospital admission to IVIg initiation and the length of stay in the hospital and ICU among the survivors. Our findings did not support the use of IVIg in combination with hydroxychloroquine and lopinavir/ritonavir in treatment of severe COVID-19 cases.


Findings: Arterial and venous thrombosis are common in COVID-19, especially in critically ill patients. Thromboprophylaxis should be considered for all hospitalized patients with COVID-19 in the absence of contraindications. Ongoing investigation will determine optimal preventive regimens in COVID-19 in the intensive care unit, at hospital discharge, and in nonhospitalized patients at high-risk for thrombosis.

Findings: In this retrospective study, all critically ill COVID-19 patients admitted to two intensive care units in March and April 2020 were eligible. A total of 152 patients were included: 67 received low-, 48 medium-, and 37 high-dose thromboprophylaxis. Baseline characteristics did not differ between groups. For patients who received high-dose prophylaxis, mortality was lower (13.5%) compared to those who received medium dose (25.0%) or low dose (38.8%), p = 0.02. The hazard ratio of death was 0.33 among those who received high dose, and 0.88 among those who received medium dose, as compared to those who received low-dose thromboprophylaxis. There were fewer thromboembolic events in the high (2.7%) vs medium (18.8%) and low-dose thromboprophylaxis (17.9%) groups, p = 0.04. Among critically ill COVID-19 patients with respiratory failure, high-dose thromboprophylaxis was associated with a lower risk of death and a lower cumulative incidence of thromboembolic events compared with lower doses.

Transmission / Infection Control


Findings: We used a quantitative microbial risk assessment (QMRA) approach to relate log10 disinfection reductions of SARS-CoV-2 bioburden to COVID-19 infection risks. Under low viral bioburden, minimal log10 reductions may be needed to reduce infection risks for a single hand-to-fomite touch to levels lower than 1:1,000,000, as a risk comparison point. For higher viral bioburden conditions, log10 reductions of more than 2 may be needed to achieve median infection risks of less than 1:1,000,000.


Findings: A total of 3030 participants were randomly assigned to the recommendation to wear masks, and 2994 were assigned to control; 4862 completed the study. Infection with SARS-CoV-2 occurred in 42 participants recommended masks (1.8%) and 53 control participants (2.1%). The between-group difference was −0.3 percentage point. The recommendation to wear surgical masks to supplement other public health measures did not reduce the SARS-CoV-2 infection rate among wearers by more than 50% in a community with modest infection rates, some degree of social distancing, and uncommon general mask use. The data were compatible with lesser degrees of self-protection.


Findings: We collected 100 air samples in acute care hospital rooms hosting 22 patients over the course of nearly two months using three different air samplers with multiple flow rates and elution protocols. Quantification by RT-qPCR (ORF1b) led to 11 positive samples from 6 patient rooms (Ct < 40). Viral cultures from the samples were negative. No correlation was observed between particular symptoms, length of hospital stay, clinical parameters, and time since symptom onset and the detection of viral RNA in the air. Low detection rates in the hospital rooms may be attributable to the appropriate application of mitigation methods according to the risk control hierarchy, such as increased ventilation to 4.85 air changes per hour (ACPH) in order to create negative pressure rooms. Our work estimates the mean emission rate of patients and potential airborne concentration in the absence of ventilation. Additional research is needed to discover whether and how often aerosolization events occur, what factors contribute to their production, and how best to prevent them.


Findings: The high risk of bias in the trials, variation in outcome measurement, and relatively low compliance with the interventions during the studies hamper drawing firm conclusions and generalising the findings to the current COVID-19 pandemic. There is uncertainty about the effects of face masks. The low-moderate certainty of the evidence means our confidence in the effect estimate is limited, and that the true effect may be different from the observed estimate of the effect. The pooled results of randomised trials did not show a clear reduction in respiratory viral infection with the use of medical/surgical masks during seasonal influenza. There were no clear differences between the use of medical/surgical masks compared with N95/P2 respirators in healthcare workers when used in routine care to reduce respiratory viral infection. Hand hygiene is likely to modestly reduce the burden of respiratory illness. Harms associated with physical interventions were under-investigated. There is a need for large, well-designed RCTs addressing the effectiveness of many of these interventions in multiple settings and populations, especially in those most at risk of ARIs.

Vaccine


FINDINGS: Between May 30 and Aug 8, 2020, 560 participants were enrolled: 160 aged 18-55 years (100 assigned to ChAdOx1 nCoV-19, 60 assigned to MenACWY), 160 aged 56-69 years (120 assigned to ChAdOx1 nCoV-19: 40 assigned to MenACWY), and 240 aged 70 years and older (200 assigned to ChAdOx1 nCoV-19: 40 assigned to MenACWY). Seven participants did
not receive the boost dose of their assigned two-dose regimen, one participant received the incorrect vaccine, and three were excluded from immunogenicity analyses due to incorrectly labelled samples. 280 (50%) of 552 analysable participants were female. Local and systemic reactions were more common in participants given ChAdOx1 nCoV-19 than in those given the control vaccine, and similar in nature to those previously reported (injection-site pain, feeling feverish, muscle ache, headache), but were less common in older adults (aged ≥56 years) than younger adults. In those receiving two standard doses of ChAdOx1 nCoV-19, after the prime vaccination local reactions were reported in 43 (88%) of 49 participants in the 18-55 years group, 22 (73%) of 30 in the 56-69 years group, and 30 (61%) of 49 in the 70 years and older group, and systemic reactions in 42 (86%) participants in the 18-55 years group, 23 (77%) in the 56-69 years group, and 32 (65%) in the 70 years and older group. As of Oct 26, 2020, 13 serious adverse events occurred during the study period, none of which were considered to be related to either study vaccine. In participants who received two doses of vaccine, median anti-spike SARS-CoV-2 IgG responses 28 days after the boost dose were similar across the three age cohorts (standard-dose groups: 18-55 years, 20 713 arbitrary units [AU]/mL [IQR 13 898-33 550], n=39; 56-69 years, 16 170 AU/mL [10 233-40 353], n=26; and ≥70 years 17 561 AU/mL [9705-37 796], n=47; p=0.68). Neutralising antibody titres after a boost dose were similar across all age groups (median MNA80 at day 42 in the standard-dose groups: 18-55 years, 193 [IQR 113-238], n=39; 56-69 years, 144 [119-347], n=20; and ≥70 years, 161 [73-323], n=47; p=0.40). By 14 days after the boost dose, 208 (>99%) of 209 boosted participants had neutralising antibody responses. T-cell responses peaked at day 14 after a single standard dose of ChAdOx1 nCoV-19 (18-55 years: median 1187 spot-forming cells [SFCs] per million peripheral blood mononuclear cells [IQR 841-2428], n=24; 56-69 years: 797 SFCs [383-1817], n=29; and ≥70 years: 977 SFCs [458-1914], n=48). INTERPRETATION: ChAdOx1 nCoV-19 appears to be better tolerated in older adults than in younger adults and has similar immunogenicity across all age groups after a boost dose. Further assessment of the efficacy of this vaccine is warranted in all age groups and individuals with comorbidities.

Women & Children


Findings: Remdesivir has not been approved to treat COVID-19 in children under 12 years old, although the drug is currently being prescribed in critically ill children. Remdesivir has recently demonstrated promising results in adults with COVID-19, but few data have been reported to date in paediatric population. We report a multicentre cohort of children with confirmed SARS-CoV-2 and severe COVID-19 disease receiving remdesivir during the first month of the pandemic in Spain. • No remdesivir-related adverse outcomes were observed in most of the cases. Seven patients reached successful clinical outcome, and one died due to complications (bacterial sepsis).

Findings: From March 18 through August 22, 2020, 3374 pregnant women (mean age, 27.6 years) tested for SARS-CoV-2 were delivered, including 252 who tested positive for SARS-CoV-2 and 3122 who tested negative. The cohort included 2520 Hispanic (75%), 619 Black (18%), and 125 White (4%) women. There were no differences in age, parity, body mass index, or diabetes among women with or without SARS-CoV-2. SARS-CoV-2 positivity was more common among Hispanic women. There was no difference in the composite primary outcome. Early neonatal SARS-CoV-2 infection occurred in 6 of 188 tested infants (3%), primarily born to asymptomatic or mildly symptomatic women. There were no placental pathologic differences by illness severity. Maternal illness at initial presentation was asymptomatic or mild in 239 women (95%), and 6 of those women (3%) developed severe or critical illness. Fourteen women (6%) were hospitalized for the indication of COVID-19. In a large, single-institution cohort study, SARS-CoV-2 infection during pregnancy was not associated with adverse pregnancy outcomes. Neonatal infection may be as high as 3% and may occur predominantly among asymptomatic or mildly symptomatic women. Placental abnormalities were not associated with disease severity, and hospitalization frequency was similar to rates among nonpregnant women.

Findings: To the best of our knowledge, no longitudinal study has reported the kinetics of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody responses in children. Here we report the results of the second round of antibody testing in children from a prospective multicentre cohort study in the UK. Our results indicate that antibody titres in children exposed to SARS-CoV-2 remain at a detectable level for at least 62 days, and that in this cohort mean antibody titres increased over time. This finding is consistent with available data on antibody titres in adults.

Findings: In this cohort study using electronic health records for 135 794 US pediatric patients in 7 children’s health systems, 96% of patients tested had negative results, and rates of severe cardiorespiratory presentation of coronavirus disease 2019 (COVID-19) illness were low. Minority race/ethnicity, chronic illness, and increasing age were associated with SARS-CoV-2 infection. This study suggests that for most pediatric patients, the risk of SARS-CoV-2 infection appears low, but higher concern may be warranted for patients with medically complex conditions or those of minority race/ethnicity.

Findings: 35 articles were included in the study. Seven studies were research articles and twenty-eight were case reports. Methodological quality was medium. Most of the clinical characteristics of newborns were respiratory difficulty and secondly fever. Some newborns gastrointestinal (GIS) symptoms in the form of diarrhea and feeding intolerance and abdominal distension were present in 50%. The fatality case did not exist in any newborn due to COVID-19. Death occurred in one case due to prematurity. The most common symptoms in patients with COVID-19 infection in the neonatal period are respiratory tract symptoms and fever. It has been observed that the COVID-19 infection detected in the neonatal period is not fatal. However, data including more cases are needed.

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**GUIDELINES & CONSENSUS STATEMENTS**

*Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19.* 11-20-20 includes revisions to the sections on lopinavir/ritonavir, tocilizumab, and remdesivir.

*WHO’s Therapeutics and COVID-19: living guideline* 11-20-20

**FDA / CDC / NIH / WHO Updates**

*CDC* - [Strategies for Optimizing the Supply of N95 Respirators](https://www.cdc.gov/epidemicblo...ulated 11-23-20

*FDA* - [Authorizes First COVID-19 Test for Self-Testing at Home](https://www.fda.gov/)


*WHO* - [WHO recommends against the use of remdesivir in COVID-19 patients](https://www.who.int/)

*WHO* - [Diagnostics, therapeutics, vaccine readiness, and other health products for COVID-19](https://www.who.int/)

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**Commentary & News Releases**

*PFIZER AND BIONTECH CONCLUDE PHASE 3 STUDY OF COVID-19 VACCINE CANDIDATE, MEETING ALL PRIMARY EFFICACY ENDPOINTS*


AstraZeneca COVID vaccine latest to show high efficacy.

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