**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**

   [https://science.sciencemag.org/content/early/2021/06/30/science.abi7994](https://science.sciencemag.org/content/early/2021/06/30/science.abi7994)

   A novel variant of concern (VOC) named CAL.20C (B.1.427/B.1.429), originally detected in California, carries spike glycoprotein mutations S13I in the signal peptide, W152C in the N-terminal domain (NTD), and L452R in the receptor-binding domain (RBD). Plasma from individuals vaccinated with a Wuhan-1 isolate-based mRNA vaccine or convalescent individuals exhibited neutralizing titers, which were reduced 2-3.5 fold against the B.1.427/B.1.429 variant relative to wildtype pseudoviruses. The L452R mutation reduced neutralizing activity of 14 out of 34 RBD-specific monoclonal antibodies (mAbs). The S13I and W152C mutations resulted in total loss of neutralization for 10 out of 10 NTD-specific mAbs since the NTD antigenic supersite was remodeled by a shift of the signal peptide cleavage site and formation of a new disulphide bond, as revealed by mass spectrometry and structural studies.

   [https://pubs.rsna.org/doi/10.1148/radiol.2021210384](https://pubs.rsna.org/doi/10.1148/radiol.2021210384)

   Results Of 10,930 subjects screened for eligibility, 10,735 were included and 6,448 (60.0%) had a positive RT-PCR result. With RT-PCR as reference, the sensitivity and specificity and CT were 80.2% and 79.7%, respectively with strong agreement between junior and senior radiologists. Of all the variables analysed, the extent of pneumonia on CT was the best predictor of severe outcome at one month. Using pre-defined criteria, CT reading is not influenced by reader’s experience and helps predict the outcome at one month.

Publicly available data from The COVID Tracking Project at The Atlantic were accessed between 9 September 2020 and 14 September 2020. The Hispanic population had a median of 158% higher COVID-19 infection relative to their % population proportion. This was followed by AA, with 50% higher COVID-19 infection relative to their % population proportion. The AA population had the most disproportionate mortality, with a median of 46% higher mortality than the % population proportion. Disproportionate impact of COVID-19 was also seen in AI/AN and Asian populations, with 100% excess infections than the % population proportion seen in nine states for AI/AN and seven states for Asian populations. There was no disproportionate impact in the white population in any state.


Between 2010 and 2020, the FDA approved 21 new vaccines for use, with a median review time from submission to approval of 12 months. By permitting EUA for COVID-19 vaccines, the median review time was 21 days during the COVID-19 pandemic. Regulators have adopted new pathways and frameworks that allow for rapid vaccine authorization in specific circumstances and have acknowledged the need for more data regarding safety and efficacy to permit full approval. Medicine regulators are engaging with vaccine developers earlier; for example, HC has developed fast-track approval processes specifically for COVID-19 vaccines, which begins the review process earlier and allows evidence to be reviewed as it becomes available. Furthermore, increasing global regulatory harmonization is enabling the robust and timely approval of COVID-19 vaccines. With the potential challenges that new variants of SARS-CoV-2 may bring, the COVID-19 vaccine armamentarium will likely need further additions and requires prompt regulatory approval to ensure that we can meet the continuing challenges brought by the global pandemic.


During March 27-July 14, 2020, the CDC’s National Healthcare Safety Network extended its surveillance to hospital capacities responding to COVID-19 pandemic. The data showed wide
variations across hospitals in case burden, bed occupancies, ventilator usage, and healthcare personnel and supply status. These data were used to inform emergency responses.

Prognosis


   A higher sequential organ failure assessment score and acute physiology and chronic health evaluation-2 score; a lower PaO2 :FiO2 and the need for mechanical ventilation at admission were associated with mortality. Increasing age, pre-existing comorbidities, severity of illness based on validated scoring systems, and the host response to the disease were associated with mortality; while male sex and increasing BMI were not. These factors have prognostic relevance for patients admitted to intensive care with COVID-19.


   This study included 300 participants with nucleic acid test-confirmed COVID-19. Plasma SARS-CoV-2 viremia levels at the time of presentation predicted adverse disease outcomes. Proteomic analyses revealed prominent proteomic pathways associated with SARS-CoV-2 viremia, including upregulation of SARS-CoV-2 entry factors (ACE2, CTSL, FURIN), heightened markers of tissue damage to the lungs, gastrointestinal tract, and endothelium/vasculature, and alterations in coagulation Pathways. CONCLUSION These results highlight the cascade of vascular and tissue damage associated with SARS-CoV-2 plasma viremia that underlies its ability to predict COVID-19 disease outcomes.

Survivorship & Rehabilitation


   Consistent with previous research, family members of critical care survivors in this cohort experienced high levels of anxiety and depression following discharge. Carer strain was higher in this cohort compared to previously reported cohorts. Although the psychosocial burden of COVID-19 family members may appear similar to other family member cohorts following critical care, the symptom trajectory of this unique cohort remains poorly characterised. Previous research has shown that family members’ psychosocial problems often improve over time. However, the COVID-19 family cohort is distinctive; not only did family members have less access while the patients were in hospital, but the usual support mechanisms, primarily other family and friends, have also been unavailable or inaccessible due to public health lockdowns and social restrictions.
Therapeutics


Our meta-analysis demonstrated that prone position improved PaO₂/FiO₂ ratio with better SpO₂ than supine position in COVID-19 patients. Given the limited number of studies with small sample size and substantial heterogeneity of measured outcomes, further studies are warranted to standardize the regime of prone position to improve the certainty of evidence.


In comparison to SOC or placebo, IVM did not reduce all-cause mortality, length of stay or viral clearance in RCTs in COVID-19 patients with mostly mild disease. IVM did not have an effect on AEs or severe AEs. IVM is not a viable option to treat COVID-19 patients.

Transmission / Infection Control


A simulated infected meeting participant who was exhaling aerosols was placed in a room with two simulated uninfected participants and a simulated uninfected speaker. Using two HEPA air cleaners close to the aerosol source reduced the aerosol exposure of the uninfected participants and speaker by up to 65%. A combination of HEPA air cleaners and universal masking reduced exposure by up to 90%. Portable HEPA air cleaners can reduce exposure to simulated SARS-CoV-2 aerosols in indoor environments, especially when combined with universal masking.

Vaccines / Immunology


The Comirnaty® COVID-19 vaccine elicits robust SARS-CoV-2-S antibody responses in nursing home residents. Nevertheless, the rate and frequency of detectable SARS-CoV-2 IFN-γ T-cell responses after vaccination was lower in nursing home residents compared to controls.

13. **Vaccine effectiveness of the first dose of ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of long-term care facilities in England (VIVALDI): a prospective cohort study.**
Single-dose vaccination with BNT162b2 and ChAdOx1 vaccines provides substantial protection against infection in older adults from 4-7 weeks after vaccination and might reduce SARS-CoV-2 transmission. However, the risk of infection is not eliminated, highlighting the ongoing need for non-pharmaceutical interventions to prevent transmission in long-term care facilities.


One dose of either BNT162b2 or ChAdOx1 nCoV-19 resulted in substantial risk reductions of COVID-19-related hospitalisation in people aged at least 80 years.


An mRNA vaccine boost led to a high seroconversion rate, reinforcing the need not to delay the second dose. However, anti-spike antibody titers were 3-10 times lower in patients with SCs than in healthy controls, raising concerns about impaired humoral immunity, especially in patients treated by chemotherapy. At the same time, the seroconversion data are rather reassuring among patients on anti-HER2, anti PD-1/PD-L1, antiangiogenic treatment or hormone therapy without associated chemotherapy.


Our studies demonstrate that SARS-CoV-2 mRNA-based vaccination of humans induces a persistent GC B cell response, enabling the generation of robust humoral immunity.


BNT162b2 given as a second dose in individuals prime vaccinated with ChAdOx1-S induced a robust immune response, with an acceptable and manageable reactogenicity profile.

Analysis of the results of our questionnaire demonstrate that adverse events of COVID-19 vaccinations in patients with autoimmune diseases are comparable with controls, independent of the type of vaccine. The observed adverse events consisted of expected transient local or systemic reactions that were mostly self-limiting. The frequency of participants who reported adverse events was lower than that reported in clinical trials, but similar to a nationwide observational study on adverse events of COVID-19 vaccinations in the general population done in the UK. Our data are consistent with previous studies that reported higher frequencies of adverse events in women and younger people. We did not observe any serious adverse events, but the number of participants included in our study was too low to draw conclusions about rare serious events.


Two reports in the current issue of JAMA Cardiology describe cases of acute myocarditis that occurred among persons who received the BNT162b2-mRNA (Pfizer-BioNTech) or mRNA-1273 (Moderna) messenger RNA (mRNA)–based COVID-19 vaccines authorized for use in the US.1,2 During the clinical evaluations of these patients, alternative etiologies for myocarditis were not detected.


Vaccinees' neutralization titres exceeded those of recovered non-hospitalized COVID-19 patients. Our work provides evidence that the second dose of the BNT162b2 vaccine induces cross-neutralization of at least some of the circulating SARS-CoV-2 variants.


https://www.nature.com/articles/s41586-021-03739-1

Although two-dose mRNA vaccination provides excellent protection against SARS-CoV-2, data are scarce on vaccine efficacy against variants of concern (VOC) in individuals above 80 years of age. We conclude that the elderly are a high risk population that warrant specific measures to boost vaccine responses, particularly where variants of concern are circulating.


Authorized mRNA vaccines were highly effective among working-age adults in preventing SARS-CoV-2 infection when administered in real-world conditions, and the vaccines attenuated the viral RNA load, risk of febrile symptoms, and duration of illness among those who had breakthrough infection despite vaccination. (Funded by the National Center for Immunization and Respiratory Diseases and the Centers for Disease Control and Prevention.).


A two-dose regimen of the NVX-CoV2373 vaccine administered to adult participants conferred 89.7% protection against SARS-CoV-2 infection and showed high efficacy against the B.1.1.7 variant.


These data show that B cell depletion completely blocks humoral but not T cell SARS-CoV-2 vaccination response. Furthermore, limited humoral immune responses are found in B cell depleted patients after SARS-CoV-2 infection.

Women & Children


In this nationwide study of pregnant people in the U.S., the risk of pregnancy loss at <20 weeks gestation was about 6%, both for participants with COVID-19 (N=94) and COVID-19 negative controls (N=15). This data compares favorably to the 10% rate of miscarriage among clinically recognized first trimester pregnancies prior to the pandemic. To our knowledge, this is the largest analyses of COVID-19 in the first trimester in a U.S. longitudinal cohort. With this sample size, the upper bound of the confidence interval for pregnancy loss of 13.4% is reassuring because it is not significantly higher than the expected miscarriage rate without viral infection. These results can guide counseling for people infected with SARS-CoV-2 early in pregnancy.


COVID-19 during pregnancy is strongly associated with preeclampsia, especially among nulliparous women. This association is independent of any risk factors and preexisting conditions. COVID-19 severity does not seem to be a factor in this association. Both conditions are associated independently of and in an additive fashion with preterm birth, severe perinatal morbidity and mortality, and adverse maternal outcomes. Women with preeclampsia should be considered a particularly vulnerable group with regard to the risks posed by COVID-19.

SARS-CoV-2 was common among young infants hospitalized for SBI evaluation during periods of high, but not low, community SARS-CoV-2 circulation in New York City, although most infants did not require intensive care admission.


Our data reinforce the need to recognise the increased protection offered by a second vaccine dose as COVID-19 cases associated with the B.1.617.2 variant increase. They also suggest that further booster immunisations might be needed, especially for more susceptible groups that have received vaccines that induce lower than average NAbTs. As with mRNA vaccines, it might be feasible to prioritise the use of the AZD1222 vaccine, in light of severely restricted supply, for people with a confirmed history of COVID-19. Overall, our findings highlight the urgent need for expanded serological monitoring of NAbTs within sub-populations.

**GUIDELINES & CONSENSUS STATEMENTS**


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

*FDA Revokes Emergency Use Authorizations for Certain Respirators and Decontamination Systems as Access to N95s Increases Nationwide*, 6-30-21

**Commentary & News**


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