New Research
*note, PREPRINTS have not undergone formal peer review

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

Clinical Syndrome


   We conducted study from an international, multicentre, prospective cohort study of elective and emergency patients undergoing surgery during October 2020. The primary outcome measure was venous thromboembolism within 30 days of surgery. SARS-CoV-2 diagnosis was defined as peri-operative (7 days before to 30 days after surgery); recent (1-6 weeks before surgery); previous (≥7 weeks before surgery); or none. Patients undergoing surgery with peri-operative or recent SARS-CoV-2 appear to be at increased risk of postoperative venous thromboembolism compared with patients with no history of SARS-CoV-2 infection. Optimal venous thromboembolism prophylaxis and treatment are unknown in this cohort of patients, and these data should be interpreted accordingly.

Diagnostics & Screening


   Our data suggest that the use of rapid antigen testing only appears appropriate in high prevalence/incidence situations, because a (too) low prevalence may increase the risk of false-positive results leading to unnecessary quarantine and high economic burden. As the prevalence and the morbidity from Covid-19 decreases due to vaccination coverage and seasonal effects, and in parallel the results of false positive results increases, the negative consequences from false positive results become more and more important. Consequently, the question arises whether a universal population screening of asymptomatic people is a reasonable measure or if the antigen testing strategy should be considered more strongly to the incidence to increase the PPV and to improve cost-effectiveness, especially as PCR-based
test strategies appear feasible in low incidence situations regarding laboratory capacities in western countries.

**Epidemiology & Public Health**


The pandemic in the US during 2020 was characterized by national ascertainment rates that increased from 11.3% during March to 24.5% during December. Population susceptibility at year’s end was 69.0%, indicating that roughly one third of the US population had been infected. Community infectious rates, the percentage of people harbouring a contagious infection, rose above 0.8% before the end of the year, and were as high as 2.4% in some major metropolitan areas. In contrast, the infection fatality rate fell to 0.3% by year’s end.


Of 1155 participants, 1074 responded to at least 1 question. Respondents identified as male (n = 526 [49.0%]), and non-Hispanic–White individuals (n = 661 [61.7%]), with a mean age of 19.3 years. Overall 75% of respondents were interested in getting vaccinated to protect themselves and return to normal Most were concerned about adverse effects (422 [41.8%]) and the effectiveness if the vaccine (118 [11.7%]), whereas 324 (32.1%) had no concerns. 72.8% believed the vaccines are safe and/or effective, citing their trust in science (145 [20.1%]) and data (221 [30.7%]). To facilitate vaccination, youths indicated that they seek an easy sign-up process. Most youth also reported that they will continue mitigating behaviors such as wearing a mask even after vaccination.


In 108 households (n=474, 280 ≤ 18 years old), SARS-CoV-2 seroprevalence was significantly associated with age (range 37.5 -78.7%) and lowest in children ≤ 10 years old. Among 92 households with members ≤ 18, 14 (15.2%) had only a seropositive child or adolescent, while 16 (17.4%) had only seropositive adults. Households with both groups concurrently seropositive (n=62) were larger in size (mean 8.11 +/- 2.49) vs. (mean 5.77 +/- 2.31).

There was a signal toward increased severity associated with B.1.617.2. The association of B.1.617.2 with lower Ct value and longer viral shedding provides a potential mechanism for increased transmissibility.


We conducted a broad survey of US adults (N = 1,950) in order to better understand vaccine beliefs. The survey results suggested that Black and Hispanic individuals were less willing than Whites to receive the vaccine. US Blacks and Hispanics also planned to delay receiving the COVID-19 vaccine for a longer time period than Whites, potentially further increasing the risk of contracting COVID-19 within populations that are already experiencing high disease prevalence. Black respondents were less likely to want the COVID-19 vaccine at all compared with Whites and Hispanics, and mistrust of the vaccine among Black respondents was significantly higher than other racial/ethnic groups. Encouragingly, many Black and Hispanic respondents reported that COVID-19 vaccine endorsements from same-race medical professionals would increase their willingness to receive it. These respondents said they would also be motivated by receiving more information on the experiences of vaccine study participants who are of their own race and ethnicity.


These infection and hospitalization rate data indicate that authorized vaccines were protective against SARS-CoV-2 infection and severe COVID-19 during a period when transmission of the Delta variant was increasing. Efforts to increase COVID-19 vaccination, in coordination with other prevention strategies, are critical to preventing COVID-19-related hospitalizations and deaths.


Currently authorized vaccines have high effectiveness against COVID-19 hospitalization, but effectiveness against new cases appears to have declined in recent months, coinciding with the Delta variant's increase from <2% to >80% in the U.S. region that includes New York and relaxation of masking and physical distancing recommendations. To reduce new COVID-19 cases and hospitalizations, these findings support the implementation of a layered approach centered on vaccination, as well as other prevention strategies such as masking and physical distancing.
Healthcare Delivery & Healthcare Workers


In a large system-wide healthcare personnel (HCP) testing experience using SARS-CoV-2 PCR and serologic testing early in the COVID-19 pandemic, we did not find increased infection risk related to COVID-19 patient contact. Our findings support workplace policies for HCP protection and underscore the role of community exposure and asymptomatic infection.


During December 14, 2020-April 10, 2021, data from the HEROES-RECOVER Cohorts,* a network of prospective cohorts among frontline workers, showed that the Pfizer-BioNTech and Moderna mRNA COVID-19 vaccines were approximately 90% effective in preventing symptomatic and asymptomatic infection with SARS-CoV-2, the virus that causes COVID-19, in real-world conditions. This report updates vaccine effectiveness (VE) estimates including all COVID-19 vaccines available through August 14, 2021 and examines whether VE differs for adults with increasing time since completion of all recommended vaccine doses. VE before and during SARS-CoV-2 B.1.617.2 (Delta) variant predominance, which coincided with an increase in reported COVID-19 vaccine breakthrough infections, were compared.

Prognosis


Chronic comorbidities, complications, and demographic variables including acute kidney injury, COPD, diabetes, hypertension, CVD, cancer, increased D-dimer, male gender, older age, current smoker, and obesity are clinical risk factors for a fatal outcome associated with coronavirus.

Survivorship & Rehabilitation


A total of 18,251 publications were identified, of which 15 met the inclusion criteria. The prevalence of 55 long-term effects was estimated, 21 meta-analyses were performed, and 47,910 patients were included (age 17-87 years). The included studies defined long-COVID as
ranging from 14 to 110 days post-viral infection. It was estimated that 80% of the infected patients with SARS-CoV-2 developed one or more long-term symptoms. The five most common symptoms were fatigue (58%), headache (44%), attention disorder (27%), hair loss (25%), and dyspnea (24%). Multi-disciplinary teams are crucial to developing preventive measures, rehabilitation techniques, and clinical management strategies with whole-patient perspectives designed to address long COVID-19 care.


Quality of life deficit was reported to be 67.7% among Covid-19 survivors with olfactory dysfunction.


A significant proportion of non-hospitalized COVID-19 patients, regardless of age, have not returned to their usual health three to eight months after infection.

**Therapeutics**


1,138 patients were enrolled including 286 who received RDV, and 852 treated with BSC, 400 of whom received hydroxychloroquine. Corticosteroids were used in 20.4% of the cohort (12.6% in RDV and 23% in BSC). In persons receiving RDV compared to those receiving BSC the HR (95%CI) for death was 0.46 (0.31 – 0.69) in the univariate model, p<0.001 and 0.60 (0.40 – 0.90) in the risk-adjusted model, p=0.014. In the sub-group of persons with baseline use of low-flow oxygen, the HR (95%CI) for death in RDV compared to BSC was 0.63 (0.39 – 1.00), p=0.049. Treatment with RDV was associated with lower mortality compared to BSC. These findings remain the same in the subgroup with baseline use of low-flow oxygen.

Initiation of remdesivir prior to or simultaneously with dexamethasone was associated with significantly shorter time to clinical improvement and positive IgG antibody, lower risk of in-hospital death, in addition to shorter length of hospital stay in patients with moderate COVID-19.


Awake prone positioning of patients with hypoxaemic respiratory failure due to COVID-19 reduces the incidence of treatment failure and the need for intubation without any signal of harm. These results support routine awake prone positioning of patients with COVID-19 who require support with high-flow nasal cannula.

**Transmission / Infection Control**


To investigate the evolution of SARS-CoV-2 in the immune population, we mixed the authentic virus with a highly neutralizing plasma from a COVID-19 convalescent patient. The plasma fully neutralized the virus for seven passages, but, after 45 d, the deletion of F140 in the spike N-terminal domain (NTD) N3 loop led to partial breakthrough. At day 73, an E484K substitution in the receptor-binding domain (RBD) occurred, followed, at day 80, by an insertion in the NTD N5 loop containing a new glycan sequon, which generated a variant completely resistant to plasma neutralization. Computational modeling predicts that the deletion and insertion in loops N3 and N5 prevent binding of neutralizing antibodies. The recent emergence in the United Kingdom, South Africa, Brazil, and Japan of natural variants with similar changes suggests that SARS-CoV-2 has the potential to escape an effective immune response and that vaccines and antibodies able to control emerging variants should be developed.

We instituted Personal Protective Equipment (PPE) Monitors as part of our care of COVID-19 patients in high-risk zones. PPE Monitors aided healthcare personnel (HCP) in donning and doffing, which contributed to nearly zero transmission of COVID-19 to HCP, despite their care of over 1400 COVID-19 patients.


This cohort study found that individuals with COVID-19 were most infectious a few days before and after symptom onset. Infected contacts of asymptomatic index patients were less likely to present with COVID-19 symptoms, suggesting that quantity of exposure may be associated with clinical presentation in close contacts.

Vaccines / Immunology


We conducted a retrospective observational study comparing three groups: (1)SARS-CoV-2-naïve individuals who received a two-dose regimen of the BioNTech/Pfizer mRNA BNT162b2 vaccine, (2)previously infected individuals who have not been vaccinated, and (3)previously infected and single dose vaccinated individuals. We evaluated four outcomes: SARS-CoV-2 infection, symptomatic disease, COVID-19-related hospitalization and death. The follow-up period of June 1 to August 14, 2021, when the Delta variant was dominant in Israel.

Results: SARS-CoV-2-naïve vaccinees had a 13.06-fold increased risk for breakthrough infection with the Delta variant compared to those previously infected, when the first event (infection or vaccination) occurred during January and February of 2021. The increased risk was significant for symptomatic disease as well. When allowing the infection to occur at any time before vaccination (from March 2020 to February 2021), evidence of waning natural immunity was demonstrated, though SARS-CoV-2 naïve vaccinees had a 5.96-fold increased risk for breakthrough infection and a 7.13-fold increased risk for symptomatic disease. SARS-CoV-2-naïve vaccinees were also at a greater risk for COVID-19-related-hospitalizations compared to those that were previously infected. This study demonstrated that natural immunity confers longer lasting and stronger protection against infection, symptomatic disease and hospitalization caused by the Delta variant of SARS-CoV-2, compared to the BNT162b2 two-dose vaccine-induced immunity. Individuals who were both previously infected with SARS-CoV-2 and given a single dose of the vaccine gained additional protection against the Delta variant.

In this study in a nationwide mass vaccination setting in Israel, the BNT162b2 vaccine was not associated with an elevated risk of most of the adverse events examined. The vaccine was associated with an excess risk of myocarditis (1 to 5 events per 100,000 persons). The risk of this potentially serious adverse event and of many other serious adverse events was substantially increased after SARS-CoV-2 infection.


In this observational study, we found that patients with RMD who received J&J vaccination had a lower rate of seroconversion compared with recipients of the mRNA series. One in five participants who received J&J vaccination did not mount a detectable antibody response. In those with a detectable antibody response, participants who received the J&J vaccine had lower antibody titres than the mRNA group. While no cut-off titre has been defined to associate with protection, there is a well-recognised role of neutralising antibodies in protection against SARS-CoV-2 infection.


Effectiveness of mRNA vaccines against COVID-19-associated hospitalization was sustained over a 24-week period, including among groups at higher risk for severe COVID-19; ongoing monitoring is needed as new SARS-CoV-2 variants emerge. To reduce their risk for hospitalization, all eligible persons should be offered COVID-19 vaccination.


These findings indicate that mRNA vaccines provide protection against SARS-CoV-2 infection among nursing home residents; however, VE was lower after the Delta variant became the predominant circulating strain in the United States. This analysis assessed VE against any infection, without being able to distinguish between asymptomatic and symptomatic presentations. Additional evaluations are needed to understand protection against severe disease in nursing home residents over time. Because nursing home residents might remain at some risk for SARS-CoV-2 infection despite vaccination, multiple COVID-19 prevention strategies, including infection control, testing, and vaccination of nursing home staff members, residents, and visitors, are critical. An additional dose of COVID-19 vaccine might be considered for nursing home and long-term care facility residents to optimize a protective immune response.

Although our review does not reveal serious safety signals, available data have serious limitations and are insufficient to delineate the complete spectrum of potential adverse outcomes associated with exposure to remdesivir during pregnancy and lactation. Importantly, there are very few data on remdesivir exposure in the first trimester, when organogenesis occurs. In addition, requisite pharmacokinetic data in pregnancy are currently lacking. The role of remdesivir in preventing vertical or postnatal SARS-CoV-2 transmission is also unclear. Diligent follow-up and documentation of outcomes in pregnant people with COVID-19 treated with remdesivir will be important moving forward.


Published data on tocilizumab in pregnancy includes 610 cases (n=20 with COVID-19) together with 7 mother-infant breastfeeding pairs. Higher rates of spontaneous abortion and premature birth have been reported compared to the general population, but multiple confounding variables limit interpretation. There is little data on tocilizumab exposure in the second and third trimesters when transplacental transport is highest. The effects of tocilizumab on the developing immune system are unclear. Pregnant patients with COVID-19 who received tocilizumab were often critically ill and corticosteroid use was uncommon. Neonatal follow-up was limited. Tocilizumab appears to be compatible with breastfeeding.

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

**FDA Approves First COVID-19 Vaccine,** August 23, 2021


**Commentary**


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