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

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

Clinical Syndrome

   
   Up to one-third of COVID-19 patients analysed in this review experienced at least one neurological manifestation. One in 50 patients experienced stroke. In those over 60, more than one-third had acute confusion/delirium; the presence of neurological manifestations in this group was associated with near doubling of mortality. Results must be interpreted keeping in view the limitations of observational studies and associated bias.

   
   We encountered occasional cases of AE in our 2020 COVID-19 experience. Consistent with sporadic reports and small case series during the COVID-19 pandemic, and prior experience of postinfectious AE, our cases had diverse clinical presentations and were neural IgG and CSF viral particle negative. Application of diagnostic criteria assists in differentiation of AE from toxic-metabolic causes arising in the setting of systemic infection.

Diagnostics & Screening

   
   The clinical study revealed sensitivity of 100% and specificity of 100% for HV69/70 deletion, sensitivity of 100% and specificity of 100% for N501Y, and sensitivity of 100% and specificity of 98.10% for E484K mutation. Analytical performance demonstrated stability and reproducibility over 7 days, and LOD was calculated at 698 cp/mL for NP swab specimens, and 968 cp/mL for
SG specimens. The Allplex™ SARS-CoV-2 Variants I assay is acceptable for clinical use for the detection of variant of concern and variant of interest.

**Epidemiology & Public Health**


   In this cohort study, family members without immunity had a 45% to 97% lower risk of contracting COVID-19 as the number of immune family members increased. Vaccination is a key strategy for decreasing the transmission of the virus within families.


   We found substantial evidence of secondary infections among household contacts. People with COVID-19, particularly those with immunocompromising conditions or those with household contacts with diabetes, should take care to promptly self-isolate to prevent household transmission.


   As of 31 May, over 3 months into the pandemic, nearly 5500 positive HCWs were reported to LAC DPH, representing 9.6% of all cases. Cases reported working in 27 different setting types, including outpatient medical offices, correctional facilities, emergency medical services, and so forth, with the highest proportion from long-term care facilities (46.6%) and hospitals (27.7%). Case patients included both clinical and nonclinical roles, with nearly half (49.4%) of positive HCWs being nurses. Over two-thirds of HCWs (68.6%) worked at some point during their infectious period, and nearly half (47.9%) reported a known exposure to a positive patient and/or coworker within their facility. Overall, compared to all LAC cases, HCWs reported lower rates of hospitalization (5.3% vs 12.2%) and death (0.7% vs 4.3%) from COVID-19. There are many factors that increase HCWs risk of infection, including high-risk work environment, limited supply of personal protective equipment, and even pressure to help and work during a pandemic. In response to these data, LAC DPH created resources and provided guidance for healthcare facilities to best protect their patients and staff during the COVID-19 pandemic.


   Later statewide emergency declarations and school closure were associated with higher Covid-19 mortality. Each day of delay increased mortality risk 5 to 6%.
https://jamanetwork.com/journals/jama/fullarticle/2785290
To optimize outreach and education, understanding the degree to which an individual’s intent to vaccinate changes over time and assessing factors that relate to rising vaccine likelihood are critical. For example, whether individuals who are initially “unsure” or “unlikely” will eventually be vaccinated is unknown. Most studies of vaccine intent are cross-sectional and cannot assess these changes. Using data from a nationally representative longitudinal study of adults in the US, we assessed individual-level change in vaccine intent and uptake between April 2021 and July 2021 and characteristics of individuals who reported an increase in vaccine likelihood or uptake.

Healthcare Delivery & Healthcare Workers

Patients, families, and healthcare professionals were impacted by restricted visitation policies in acute care settings during COVID-19. The consequences of this approach on patients and families are understudied and warrant evaluation of approaches to mitigate their impact. Future pandemic policy development should include the perspectives of patients, families, and healthcare professionals.

Survivorship & Rehabilitation

https://www.thelancet.com/journals/lancres/article/PIIS2213-2600(21)00383-0/fulltext
We identified factors related to not recovering after hospital admission with COVID-19 at 6 months after discharge (e.g., female sex, middle age, two or more comorbidities, and more acute severe illness), and four different recovery phenotypes. The severity of physical and mental health impairments were closely related, whereas cognitive health impairments were independent. In clinical care, a proactive approach is needed across the acute severity spectrum, with interdisciplinary working, wide access to COVID-19 holistic clinical services, and the potential to stratify care.

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2784918
In this systematic review, more than half of COVID-19 survivors experienced PASC 6 months after recovery. The most common PASC involved functional mobility impairments, pulmonary abnormalities, and mental health disorders. These long-term PASC effects occur on a scale that
could overwhelm existing health care capacity, particularly in low- and middle-income countries.

**Therapeutics**


A total of 2,879 infused patients and matched controls were included in the analysis, including 1,718 patients infused with bamlanivimab, 346 patients infused with bamlanivimab-etesevimab, and 815 patients infused with casirivimab-imdevimab. Hospital admission and mortality rates were significantly decreased overall in mAb-infused patients relative to matched controls. Among the infused cohort, those who received casirivimab-imdevimab had significantly decreased rate of admission relative to the other two mAbs groups. Treatment with bamlanivimab, bamlanivimab-etesevimab, or casirivimab-imdevimab significantly decreased the number of patients who progressed to severe COVID-19 disease and required hospitalization.


Among symptomatic clinically stable outpatients with COVID-19, treatment with aspirin or apixaban compared with placebo did not reduce the rate of a composite clinical outcome. However, the study was terminated after enrollment of 9% of participants because of an event rate lower than anticipated.


Mortality after ECMO for patients with COVID-19 worsened during 2020. These findings inform the role of ECMO in COVID-19 for patients, clinicians, and policy makers.


In-hospital use of ARB was associated with a significant reduction in in-hospital mortality among COVID-19-positive African American patients.

Among high-risk patients with mild to moderate COVID-19, treatment with bamlanivimab was associated with a statistically significant lower rate of hospitalization, ICU admission, and mortality compared with usual care.


Subcutaneous REGEN-COV prevented symptomatic Covid-19 and asymptomatic SARS-CoV-2 infection in previously uninfected household contacts of infected persons. Among the participants who became infected, REGEN-COV reduced the duration of symptomatic disease and the duration of a high viral load. (Funded by Regeneron Pharmaceuticals and others; ClinicalTrials.gov number, NCT04452318.).


https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2784998

The approach for MAB administration has varied and is often facility specific. Strategies used have included administration in outpatient infusion centers and EDs. During the recent spring surge of 2021, the Michigan Department of Human and Health Services reported that up to 30% of patients testing positive for COVID-19 may qualify for MAB and provided a goal that at least 50% of qualifying patients receive MAB. Descriptions of novel approaches to promote MAB administration are needed. One strategy implemented by our health system is partnership with community integrated paramedics (CIP) to promote home MAB administration. This cohort study describes our experience and how this strategy may factor into associated outcomes.

**Vaccines / Immunology**

19. **Effectiveness of COVID-19 vaccines against SARS-CoV-2 infection with the Delta (B.1.617.2) variant: second interim results of a living systematic review and meta-analysis, 1 January to 25 August 2021.** Harder T, et al. *Eurosurveillance.* 26(41) 14/Oct/2021

https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.41.2100920

These second interim results of our living systematic review show that COVID-19 vaccines approved in the EU have a moderate to high effectiveness against mild to moderate forms of SARS-CoV-2 infections caused by the Delta variant, while VE against severe disease and hospitalisation was high to very high. Statistical heterogeneity was low in meta-analysis of the severe outcomes, further supporting a well-maintained effectiveness against these endpoints under Delta variant dominance.


Defining the correlates of protection necessary to manage the COVID-19 pandemic requires the analysis of both antibody and T cell parameters, but the complexity of traditional tests limits
virus-specific T cell measurements. We tested the sensitivity and performance of a simple and rapid SARS-CoV-2 spike protein-specific T cell test based on the stimulation of whole blood with peptides covering the SARS-CoV-2 spike protein, followed by cytokine (IFN-γ, IL-2) measurement in different cohorts including BNT162b2-vaccinated individuals (n = 112), convalescent asymptomatic and symptomatic COVID-19 patients (n = 130), and SARS-CoV-1-convalescent individuals (n = 12). The sensitivity of this rapid test is comparable to that of traditional methods of T cell analysis (ELISPOT, activation-induced marker). Using this test, we observed a similar mean magnitude of T cell responses between the vaccinees and SARS-CoV-2 convalescents 3 months after vaccination or virus priming. However, a wide heterogeneity of the magnitude of spike-specific T cell responses characterized the individual responses, irrespective of the time of analysis. The magnitude of these spike-specific T cell responses cannot be predicted from the neutralizing antibody levels. Hence, both humoral and cellular spike-specific immunity should be tested after vaccination to define the correlates of protection necessary to evaluate current vaccine strategies.


Findings show high VE among HCP in NYC in the pre-Delta phase, with moderate decline in VE post-Delta emergence. SARS CoV-2 clades were similarly distributed among vaccinated and unvaccinated infected HCP without apparent clustering during the pre-Delta period of diverse clade circulation. Strong vaccine protection against hospitalization was maintained through the entire study period.


Homologous and heterologous booster vaccinations were well-tolerated and immunogenic in adults who completed a primary Covid-19 vaccine regimen at least 12 weeks earlier.

Women & Children


We found substantial disparities in distributions of COVID-19-associated death of parents and caregivers across racial and ethnic groups. Children losing caregivers to COVID-19 need care and safe, stable, and nurturing families with economic support, quality childcare and evidence-based parenting support programs. There is an urgent need to mount an evidence-based comprehensive response focused on those children at greatest risk, in the states most affected.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination is associated with lower odds of severe or critical coronavirus disease 2019 (COVID-19) or COVID-19 of any severity in pregnant patients during the Delta-dominant fourth SARS-CoV-2 surge.


Symptomatic and asymptomatic children can carry high quantities of live, replicating SARS-CoV-2, creating a potential reservoir for transmission and evolution of genetic variants. As guidance around social distancing and masking evolves following vaccine uptake in older populations, a clear understanding of SARS-CoV-2 infection dynamics in children is critical for rational development of public health policies and vaccination strategies to mitigate the impact of COVID-19.

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

**CDC** - Science Brief: Evidence Used to Update the List of Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19

**FDA Briefing Document**: EUA amendment request for a booster dose of the Moderna COVID-19 Vaccine

**NIH** – Covid Treatment Guidelines, Updated COVID-19 Treatment Guidelines Panel’s Statement on the Prioritization of Anti-SARS-CoV-2 Monoclonal Antibodies for the Treatment or Prevention of SARS-CoV-2 Infection When There Are Logistical or Supply Constraints. Oct 7, 2021

**Commentary & News**

Merck and Ridgeback’s Investigational Oral Antiviral Molnupiravir Reduced the Risk of Hospitalization or Death by Approximately 50 Percent Compared to Placebo for Patients with Mild or Moderate COVID-19 in Positive Interim Analysis of Phase 3 Study

Merck and Ridgeback Announce Submission of Emergency Use Authorization Application to the U.S. FDA for Molnupiravir, an Investigational Oral Antiviral Medicine, for the Treatment of Mild-to-Moderate COVID-19 in At Risk Adults

An F.D.A. panel recommends J.&J. boosters at least two months after the first shot.
If you would like to receive a **customized COVID-19 Topic Alert** related to your specialty or area of interest, would like a **literature search** conducted, or have difficulty **accessing** any of the above articles please contact us at librarian@providence.org

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