COVID-19 Resource Desk

#137 | 12.18.2022 to 1.7.2023

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


Here, we report on the identification of a special group of nanobodies from immunized alpaca with potency against diverse VOCs including Omicron subvariants BA.1, BA.2 and BA.4/5, SARS-CoV-1, and major sarbecoviruses. Crystal structure analysis of one representative nanobody, 3-2A2-4, discovers a highly conserved epitope located between the cryptic and the outer face of the receptor binding domain (RBD), distinctive from the receptor ACE2 binding site. Cryo-EM and biochemical evaluation reveal that 3-2A2-4 interferes structural alteration of RBD required for ACE2 binding. Passive delivery of 3-2A2-4 protects K18-hACE2 mice from infection of authentic SARS-CoV-2 Delta and Omicron. Identification of these unique nanobodies will inform the development of next generation antibody therapies and design of pan-sarbecovirus vaccines.

Clinical Syndrome


Following the U.S. onset of the COVID-19 pandemic in February 2020, the NV-HAP IR increased by 25% among Veterans without COVID-19 and 108% among Veterans with COVID-19, resulting in an additional 50 NV-HAP cases and $5,042,900 in direct patient care costs 12-months post admission. This increase in NV-HAP rates could be driven by elevated risk among Veterans with COVID-19, decreased prevention measures during extreme COVID-19 related system stress, and increased patient acuity among hospitalized Veterans during the first year of the pandemic.

Diagnostics & Screening
3. **Clinical accuracy of SARS-CoV-2 rapid antigen testing in screening children and adolescents.**
From the 12th of November 2020 to the 30th of September 2022, the RDT performance was evaluated prospectively in comparison to quantitative reverse transcription polymerase chain reaction (RT-qPCR) with oropharyngeal sampling as screening test strategy for all hospitalised children and adolescents under the age of 18 in a tertiary care hospital in Bavaria/Germany.

**Epidemiology & Public Health**

4. **Early Estimates of Bivalent mRNA Vaccine Effectiveness in Preventing COVID-19-Associated Emergency Department or Urgent Care Encounters and Hospitalizations Among Immunocompetent Adults - VISION Network, Nine States, September-November 2022.**
Tenforde MW et al. *MMWR Morb Mortal Wkly Rep.* 2022 Dec 30;71(5152):1616-1624. doi: 10.15585/mmwr.mm715152e1. [https://www.cdc.gov/mmwr/volumes/71/wr/mm715152e1.htm?s_cid=mm715152e1_w](https://www.cdc.gov/mmwr/volumes/71/wr/mm715152e1.htm?s_cid=mm715152e1_w)
Bivalent vaccines administered after 2, 3, or 4 monovalent doses were effective in preventing medically attended COVID-19 compared with no vaccination and provided additional protection compared with past monovalent vaccination only, with relative protection increasing with time since receipt of the last monovalent dose. All eligible persons should stay up to date with recommended COVID-19 vaccinations, including receiving a bivalent booster dose. Persons should also consider taking additional precautions to avoid respiratory illness this winter season, such as masking in public indoor spaces, especially in areas where COVID-19 community levels are high.

5. **Early Estimates of Bivalent mRNA Vaccine Effectiveness in Preventing COVID-19-Associated Hospitalization Among Immunocompetent Adults Aged ≥65 Years - IVY Network, 18 States, September 8-November 30, 2022.**
Surie D et al. *MMWR Morb Mortal Wkly Rep.* 2022 Dec 30;71(5152):1625-1630. doi: 10.15585/mmwr.mm715152e2. [https://www.cdc.gov/mmwr/volumes/71/wr/mm715152e2.htm?s_cid=mm715152e2_w](https://www.cdc.gov/mmwr/volumes/71/wr/mm715152e2.htm?s_cid=mm715152e2_w)
When compared with unvaccinated persons, VE of a bivalent booster dose received ≥7 days before illness onset (median = 29 days) against COVID-19-associated hospitalization was 84%. Compared with persons who received ≥2 monovalent-only mRNA vaccine doses, relative VE of a bivalent booster dose was 73%. These early findings show that a bivalent booster dose provided strong protection against COVID-19-associated hospitalization in older adults and additional protection among persons with previous monovalent-only mRNA vaccination. All eligible persons, especially adults aged ≥65 years, should receive a bivalent booster dose to maximize protection against COVID-19 hospitalization this winter season. Additional strategies to prevent respiratory illness, such as masking in indoor public spaces, should also be considered, especially in areas where COVID-19 community levels are high (4,5).

6. **Effect of COVID-19 Vaccine Messaging Platforms in Emergency Departments on Vaccine Acceptance and Uptake: A Cluster Randomized Clinical Trial.**
Results of this cluster randomized clinical trial showed that with low NNT, implementation of COVID-19 vaccine messaging platforms in EDs leads to greater vaccine acceptance and uptake in unvaccinated ED patients. Broad implementation in EDs could lead to greater COVID-19 vaccine delivery to underserved populations whose primary health care access occurs in EDs.

**Healthcare Delivery & Healthcare Workers**


By identifying the contributors to burn-out in ICU nurses at a systems level, the study findings inform the design and implementation of effective interventions to prevent or mitigate pandemic-related burn-out among nurses. Regarding contributors to burn-out in nurses during the pandemic, five thematic levels emerged-personal, patient related, coworker related, organisational and societal-with each factor comprising several subthemes (eg, emotional detachment from patients, constant need to justify motives to patients' family, lack of staffing and resources, and politicisation of COVID-19 and vaccination). Participants revealed several practical interventions to help overcome burn-out, ranging from mental health coverage to educating public on the severity of the pandemic and importance of vaccination.


To date, there has been a notable lack of peer-reviewed or publicly available data documenting rates of hospital quality outcomes and patient safety events during the pandemic era. The dearth of evidence is perhaps related to the US healthcare system triaging resources towards patient care and away from reporting and research, and also reflects that data used in publicly reported hospital quality rankings and ratings typically lag 2-5 years. At our institution, a learning health system assessment is underway to evaluate how patient safety was affected by the pandemic. Here, we share and discuss early findings, noting the limitations of self-reported safety event reporting, and suggest the need for further widespread investigations at other US hospitals. During the two-year study period from 2020-2021 across three large US academic medical centers at our institution, we documented an overall rate of 25.8 safety events per 1,000 inpatient days. The rate of events meeting 'harm' criteria was 12.4 per 1,000 inpatient days, the rate of non-harm events was 11.1 per 1,000 inpatient days, and the fall rate was 2.3 per 1,000 inpatient days. This descriptive, exploratory analysis suggests that patient safety event rates at our institution did not increase over the course of the pandemic. However, increasing healthcare worker absences were non-linearly and strongly associated with patient safety event rates, which raises questions regarding the mechanisms by which patient safety event rates may be affected by staff absences during pandemic peaks.

**Prognosis**

Although risk of severe disease or death for unvaccinated inpatients with Omicron was lower than Delta, it was similar to ancestral lineages. Severe outcomes were less common in vaccinated inpatients, with no difference between Delta and Omicron infections.


In this study, prior infection with SARS-CoV-2 was not associated with death, major adverse cardiovascular events, or rehospitalization following elective major noncardiac surgery, although low event rates and wide 95% CIs do not preclude a potentially meaningful increase in overall risk.

**Survivorship & Rehabilitation**


Long-COVID is associated with a substantial increase in healthcare services utilization and direct medical costs. Our findings underline the need for timely planning and allocating resources for long-COVID patient-centered care as well as for its secondary-prevention in high-risk patients.


Among critically ill patients with COVID-19 randomized to receive 1 or more therapeutic interventions, treatment with an IL-6 receptor antagonist had a greater than 99.9% probability of improved 180-day mortality compared with patients randomized to the control, and treatment with an antiplatelet had a 95.0% probability of improved 180-day mortality compared with patients randomized to the control. Overall, when considered with previously reported short-term results, the findings indicate that initial in-hospital treatment effects were consistent for most therapies through 6 months.


We conducted a population-representative survey, June 30-July 2, 2022, of a random sample of 3,042 United States adults aged 18 years or older and weighted to the 2020 US population. An estimated 7.3% of all respondents reported long COVID, corresponding to approximately 18,828,696 adults. One-quarter (25.3%) of respondents with long COVID reported their day-to-day activities were impacted 'a lot' and 28.9% had SARS-CoV-2 infection >12 months ago. The prevalence of long COVID was higher among respondents who were female, had comorbidities or were not (versus were) boosted or not vaccinated (versus boosted).
[https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2799843](https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2799843)

Based on the change in UPSIT scores, this randomized clinical trial did not show any difference between intervention arms, but when exploring within-patient change in UPSIT as well as self-reported impression of improvement, active interventions were associated with larger improvement than controls with a potential advantage of bimodal intervention. While not definitive, these results suggest that patients with COVID-19 olfactory loss may benefit from bimodal visual-olfactory training with patient-preferred scents.


Approximately half of COVID+ participants, as compared with one-quarter of COVID- participants, had at least one SARS-CoV-2 symptom at 3 months, highlighting the need for future work to distinguish Long COVID.


Compared with controls, hospitalised patients with COVID-19 had fewer problems of constipation and hard stools at 12 months after acute infection. Patients with COVID-19 had significantly higher rates of IBS than controls.

[https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0279333](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0279333)

At 1-year, patients with COVID-19 experienced an increased risk of all-cause death and adverse CV events, including ATE, VTE, and serious cardiac arrhythmias, but not CV death.

Therapeutics


Two critically ill COVID-19 infected patients, who had exhausted all available treatment options, were treated with the small-molecule RRx-001 with subsequent improvement. RRx-001, a first-in-class small molecule with anti-inflammatory, vascular normalizing and macrophage-repolarizing properties, has been safely administered 300+ patients in clinical trials. This is the first report of RRx-001 treatment of COVID-19.

Favipiravir does not improve clinical outcomes in all patients admitted to hospital with COVID-19, however, patients younger than 60 years might have a beneficial clinical response. The indiscriminate use of favipiravir globally should be cautioned, and further high-quality studies of antiviral agents, and their potential treatment combinations, are warranted in COVID-19.


The real-world effectiveness of CAS+IMD is consistent with the efficacy for reducing all-cause mortality or COVID-19-related hospitalisation reported in clinical trials. Effectiveness is maintained across patient subgroups, including those prone to breakthrough infections, and was effective against susceptible variants including Delta.


Early administration of Nirmatrelvir in high-risk patients, compared to Sotrovimab, was associated with a faster viral clearance. This may participate to decrease transmission and prevent viral resistance.


Among adults with mild-to-moderate Covid-19 who were at risk for progression, VV116 was noninferior to nirmatrelvir-ritonavir with respect to the time to sustained clinical recovery, with fewer safety concerns.


Lopinavir/ritonavir did not significantly improve symptom resolution or reduce hospitalization in non-hospitalized participants with COVID-19.

Molnupiravir did not reduce the frequency of COVID-19-associated hospitalisations or death among high-risk vaccinated adults in the community.


To date, there has been limited experience regarding nirmatrelvir/ritonavir efficacy in patients with prolonged and/or relapsing SARS-CoV-2 infection.² Here we describe three cases of relapsing COVID-19 at the Careggi University Hospital, Florence, Italy, in patients undergoing anti-CD20 immunosuppressant therapy, who showed a successful clinical, virological and radiological response to nirmatrelvir/ritonavir treatment.

**Transmission / Infection Control**


Implementing an asymptomatic patient admission testing program can provide clinically relevant data based on the NNT, even during periods of lower transmission and among different patient populations. Limiting admission testing to non-fully vaccinated patients during periods of lower transmission may be a strategy to address resource concerns around this practice. Although the impact of such testing on healthcare-associated COVID-19 among patients and healthcare workers could not be clearly determined, these data provide important information as facilities weigh the costs and benefits of such testing.


The Society for Healthcare Epidemiology of America (SHEA) recommends against routine universal use of asymptomatic screening for SARS-CoV-2 in healthcare facilities. Specifically, preprocedure asymptomatic screening is unlikely to provide incremental benefit in preventing SARS-CoV-2 transmission in the procedural and perioperative environment when other infection prevention strategies are in place, and it should not be considered a requirement for all patients. Admission screening may be beneficial during times of increased virus transmission in some settings where other layers of controls are limited (eg, behavioral health, congregate care, or shared patient rooms), but widespread routine use of admission asymptomatic screening is not recommended over strengthening other infection prevention controls. In this commentary, we outline the challenges surrounding the use of asymptomatic screening, including logistics and costs of implementing a screening program, and adverse patient and facility consequences. We review data pertaining to the lack of substantial aerosol generation during elective controlled intubation, extubation, and other procedures, and we provide guidance for when asymptomatic screening for SARS-CoV-2 may be considered in a limited scope.

We emulated a target trial using electronic health records of US veterans who received a third dose of either BNT162b2 or mRNA-1273 vaccines between 20 October 2021 and 8 February 2022, during a period that included Delta- and Omicron-variant waves. Eligible veterans had previously completed an mRNA vaccine primary series. We matched recipients of each vaccine in a 1:1 ratio according to recorded risk factors. Each vaccine group included 65,196 persons. The excess number of events over 16 weeks per 10,000 persons for BNT162b2 compared with mRNA-1273 was 45.4 (95% CI: 19.4, 84.7) for documented infection, 3.7 (2.2, 14.1) for symptomatic COVID-19, 10.6 (5.1, 19.7) for COVID-19 hospitalization, 2.0 (-3.1, 6.3) for COVID-19 intensive care unit admission and 0.2 (-2.2, 4.0) for COVID-19 death. After emulating a second target trial of veterans who received a third dose between 1 January and 1 March 2022, during a period restricted to Omicron-variant predominance, the excess number of events over 9 weeks per 10,000 persons for BNT162b2 compared with mRNA-1273 was 63.2 (95% CI: 15.2, 100.7) for documented infection. The 16-week risks of COVID-19 outcomes were low after a third dose of mRNA-1273 or BNT162b2, although risks were lower with mRNA-1273 than with BNT162b2, particularly for documented infection.


In this large population-based cohort study, patients with cancer had greater risk of SARS-CoV-2 infection and worse outcomes than patients without cancer, and the risk was highest for patients with hematologic cancer and any patients with cancer receiving active treatment. Triple vaccination was associated with lower risk of poor outcomes.


A third dose of mRNA vaccine typically elicited a robust humoral immune response among those with primary vaccination regardless of SARS-CoV-2 infection >3 months prior to boosting. Those with infection <3 months prior to boosting did not have a significant increase in antibody concentrations in response to a booster.


The findings of this cross-sectional study suggest that COV-S antibody testing allows the identification of patients with cancer who have the lowest level of antibody-derived protection from COVID-19. This
study supports larger evaluations of SARS-CoV-2 antibody testing. Prevention of SARS-CoV-2 transmission to patients with cancer should be prioritized to minimize impact on cancer treatments and maximize quality of life for individuals with cancer during the ongoing pandemic.

32. **Update to living systematic review on effectiveness of heterologous and homologous covid-19 vaccine regimens. BMJ.** 2022 Dec 6;379:o2865. doi: 10.1136/bmj.o2865.  
[https://www.bmj.com/content/379/bmj.o2865](https://www.bmj.com/content/379/bmj.o2865)  
With more evidence added to this update, better certainty exists regarding the vaccine effectiveness of a three dose vaccine regimen against covid-19 related infections. These results show that a three dose regimen is effective in protecting against covid-19 even during outbreaks of delta and omicron variants. Consistent with the first publication, an mRNA vaccine continues to be the preferred vaccine type for a booster dose.

Women & Children

[https://doi.org/10.1001/jamanetworkopen.2022.47330](https://doi.org/10.1001/jamanetworkopen.2022.47330)  
In this study of more than 11 000 US mothers, associations between socioeconomic factors, stressful life events, and mental health sequelae were complex. Accordingly, programs, policies, and practices targeting mental health during public health crises such as the COVID-19 pandemic should consider the range and configuration of hardships in designing the most effective interventions to mitigate long-term outcomes.

[https://adc.bmj.com/content/early/2023/01/04/archdischild-2022-324656](https://adc.bmj.com/content/early/2023/01/04/archdischild-2022-324656)  
Six-months post-PCR testing, CYP who tested positive for SARS-CoV-2 had similar symptoms to those who tested negative, but test-positive CYP had higher symptom prevalence. Mental health, well-being, fatigue and health-related quality of life were similar among test-positive and test-negative CYP, and symptoms at 6 months were similar in COVID-19 vaccinated and unvaccinated.

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