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

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

Clinical Syndrome


   Based on data from a US public health surveillance system, hospitalization with COVID-19 before and during vaccine availability, vs hospitalization with influenza in 2018-2019, was significantly associated with a higher risk of venous thromboembolism within 90 days, but there was no significant difference in the risk of arterial thromboembolism within 90 days.


   In this population-based cohort study of patients with COVID-19, ambulatory COVID-19 was associated with a substantially increased risk of incident VTE, but this risk was greatly reduced in fully vaccinated people with breakthrough infection. Older age, male sex, and obesity were clinical risk factors for post-COVID-19 VTE; factor V Leiden thrombophilia was additionally associated with double the risk, comparable with the risk of 10-year aging. These findings may reinforce the need for vaccination, inform VTE risk stratification, and call for targeted VTE prophylaxis strategies for unvaccinated outpatients with COVID-19.

Healthcare Delivery & Healthcare Workers


   Health care workers (HCWs) are at increased risk for acquiring SARS-CoV-2 infection, raising the issue of adequate protective measures. Although scientific evidence regarding the benefit of respirator vs surgical masks is sparse, a previous study has suggested that respirator masks (ie, FFP2) may offer additional protection to HCW with frequent COVID-19-patient exposure. In this follow-up study, we
analyzed the SARS-CoV-2 risk for HCWs depending on cumulative exposure to patients with COVID-19 and assessed whether this risk can be modulated by the use of respirator compared with surgical masks.


Survivors of COVID-19 may present with long-lasting symptoms. Some factors have been associated with the development of post-COVID conditions (also referred to as “long COVID”), including hospitalization. A study of older US veterans showed 15% reduction of long COVID after vaccination; however, study limitations included the low number of women and suboptimal vaccination schedules.

**Survivorship & Rehabilitation**


This cohort study documented an excess health care burden of PCC in the 6 months after the acute stage of infection. As health care systems evolve during a highly dynamic and ongoing global pandemic, these data provide valuable evidence to inform long-term strategic resource allocation for patients previously infected with SARS-CoV-2.


The literature on the treatment of anosmia and hyposmia includes randomized trials showing the efficacy of a few modalities. While further research is needed to expand therapeutic options for this debilitating condition, the current literature supports the use of olfactory training and topical corticosteroids.

**Therapeutics**


In this randomized clinical trial including outpatients with asymptomatic and low-risk symptomatic SARS-CoV-2, all IV and SC doses of casirivimab and imdevimab comparably reduced viral load.

clinically relevant plasma concentrations with target engagement. The data support larger clinical trials to determine clinical efficacy.

**Vaccines / Immunology**


COVID-19 mRNA vaccines have a good safety profile in pregnancy. These data can be used to appropriately inform pregnant people regarding reactogenicity of COVID-19 vaccines during pregnancy, and should be considered alongside effectiveness and immunogenicity data to make appropriate recommendations about best use of COVID-19 vaccines in pregnancy.


Administration of a booster dose of NVX-CoV2373 resulted in an incremental increase in reactogenicity. For both the prototype strain and all variants evaluated, immune responses following the booster were similar to or higher than those associated with high levels of efficacy in phase 3 studies of the vaccine. These data support the use of NVX-CoV2373 in booster programmes.


SARS-CoV-2 Omicron (B.1.1.529) BA.4 and BA.5 sub-lineages, first detected in South Africa, have changes relative to Omicron BA.1 including substitutions in the spike receptor binding domain. Here we isolated live BA.4 and BA.5 viruses and measured BA.4/BA.5 neutralization elicited by BA.1 infection either in the absence or presence of previous vaccination as well as from vaccination without BA.1 infection. In BA.1-infected unvaccinated individuals, neutralization relative to BA.1 declines 7.6-fold for BA.4 and 7.5-fold for BA.5. In vaccinated individuals with subsequent BA.1 infection, neutralization relative to BA.1 decreases 3.2-fold for BA.4 and 2.6-fold for BA.5. The fold-drop versus ancestral virus neutralization in this group is 4.0-fold for BA.1, 12.9-fold for BA.4, and 10.3-fold for BA.5. In contrast, BA.4/BA.5 escape is similar to BA.1 in the absence of BA.1 elicited immunity: fold-drop relative to ancestral virus neutralization is 19.8-fold for BA.1, 19.6-fold for BA.4, and 20.9-fold for BA.5. These results show considerable escape of BA.4/BA.5 from BA.1 elicited immunity which is moderated with vaccination and may indicate that BA.4/BA.5 may have the strongest selective advantage in evading neutralization relative to BA.1 in unvaccinated, BA.1 infected individuals.

Heterologous prime/boost vaccination with a vector-based approach (ChAdOx-1nCov-19, ChAd) followed by an mRNA vaccine (e.g. BNT162b2, BNT) has been reported to be superior in inducing protective immunity compared to repeated application of the same vaccine. However, data comparing immunity decline after homologous and heterologous vaccination as well as effects of a third vaccine application after heterologous ChAd/BNT vaccination are lacking. Here we show longitudinal monitoring of ChAd/ChAd (n = 41) and ChAd/BNT (n = 88) vaccinated individuals and the impact of a third vaccination with BNT. The third vaccination greatly augments waning anti-spike IgG but results in only moderate increase in spike-specific CD4 + and CD8 + T cell numbers in both groups, compared to cell frequencies already present after the second vaccination in the ChAd/BNT group. More importantly, the third vaccination efficiently restores neutralizing antibody responses against the Alpha, Beta, Gamma, and Delta variants of the virus, but neutralizing activity against the B.1.1.529 (Omicron) variant remains severely impaired. In summary, inferior SARS-CoV-2 specific immune responses following homologous ChAd/ChAd vaccination can be compensated by heterologous BNT vaccination, which might influence the choice of vaccine type for subsequent vaccination boosts.


During May 17-July 31, 2022, approximately 657,302 U.S. children aged 5-11 years received a third Pfizer-BioNTech dose (either a third primary series dose administered to immunocompromised children or a booster dose administered to immunocompetent children); 3,249 Pfizer-BioNTech third doses were reported to v-safe for children in this age group. Local and systemic reactions were reported to v-safe after a second dose and a third dose with similar frequency; some reactions (e.g., pain) were reported to be moderate or severe more frequently after a third dose. VAERS received 581 reports of adverse events after receipt of a Pfizer-BioNTech third dose by children aged 5-11 years; 578 (99.5%) reports were considered nonserious, and the most common events reported were vaccine administration errors. Three (0.5%) reports were considered serious; no reports of myocarditis or death were received. Local and systemic reactions were common among children after Pfizer-BioNTech third dose vaccination, but reports of serious adverse events were rare. Initial safety findings are consistent with those of the clinical trial.


We conducted a case-control study to evaluate the risk of severe complications and mortality following 1-3 doses of CoronaVac and BNT162b2 using electronic health records database. Cases were adults with their first COVID-19-related mortality or severe complications between 1 January and 31 March 2022, matched with up-to 10 controls by age, sex, index date and Charlson Comorbidity Index. Vaccine
effectiveness against COVID-19-related mortality and severe complications by type and number of doses was estimated using conditional logistic regression adjusted for comorbidities and medications. Vaccine effectiveness (95% CI) against COVID-19-related mortality after two doses of BNT162b2 and CoronaVac were 90.7% and 74.8% in those aged ≥65, 87.6% and 80.7% in those aged 50-64, 86.6% and 82.7% in those aged 18-50. Vaccine effectiveness against severe complications after two doses of BNT162b2 and CoronaVac were 82.1% and 58.9% in those aged ≥65, 83.0% and 67.1% in those aged 50-64, 78.3% and 77.8% in those aged 18-50. Further risk reduction with the third dose was observed especially in those aged ≥65 years, with vaccine effectiveness of 98.0% for BNT162b2 and 95.5% for CoronaVac against mortality, 90.8% and 88.0% against severe complications. The findings show that both CoronaVac and BNT162b2 vaccination were effective against COVID-19-related mortality and severe complications amidst the Omicron BA.2 pandemic, and risks decreased further with the third dose.

**Women & Children**


Reports of heterogeneous symptoms related to menstruation or vaginal bleeding after COVID-19 vaccination are being submitted to v-safe, although this study is unable to characterise the relationship of these symptoms to COVID-19 vaccination. Methods that leverage pretrained models to interpret and classify unsolicited signs and symptoms in free-text reports offer promise in the initial evaluation of unexpected adverse events potentially associated with use of newly authorised or licensed vaccines.


This cohort study found that the SARS-CoV-2 Delta variant was associated with higher rates of SMM events compared with other strains. Given the potential of new strains, these findings underscore the importance of preventive measures.


Of 2,326 patients who tested positive for SARS-CoV-2 during pregnancy and were at least 20 weeks' gestation at delivery from March through December 2020, 402 patients (delivering 414 fetuses/neonates) were SARS-CoV-2 positive before 28 weeks' gestation and prior to their admission for delivery; they were compared to 11,705 patients without a positive SARS-CoV-2 test. In adjusted analyses, those with SARS-CoV-2 prior to 28 weeks' had a subsequent increased risk of fetal/neonatal death [2.9% vs 1.5%, adjusted relative risk (aRR) 1.97, 95% confidence interval (CI),1.01 - 3.85],
preterm birth <37 weeks' (19.6% vs 13.8%, aRR, 1.29; 95%CI, 1.02 - 1.63) and hypertensive disorders of pregnancy with delivery less than 37 weeks' gestation (7.2% vs 4.1%, aRR 1.74, 95% CI 1.19-2.55). There were no significant differences in the rates of preterm birth <34 weeks', any major congenital malformation, size for gestational age less than the 5th or 10th percentiles. There were also no significant differences in the rate of gestational hypertension overall or in preeclampsia with severe features.

CONCLUSION: There is a modest increase in risk of adverse pregnancy outcomes subsequent to SARS-CoV-2 infection.


In ICU, corticosteroids, tocilizumab and prone positioning were used in few pregnant women with COVID-19. Over a third of patients were intubated and delivery improved the driving pressure.


The findings suggest that vaccination against covid-19 during pregnancy is not associated with a higher risk of preterm birth, small for gestational age at birth, or stillbirth.

GUIDELINES & CONSENSUS STATEMENTS


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