**COVID-19 Resource Desk**

#107 | 5.15.2022 to 5.21.2022

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Retraction Watch

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**New Research**

*note, PREPRINTS have not undergone formal peer review

COVID-19 related publications by Providence caregivers – see [Digital Commons](https://digitalcommons.providence.org)

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**Basic Science / Virology / Pre-clinical**

   [https://wwwnc.cdc.gov/eid/article/28/7/22-0526_article](https://wwwnc.cdc.gov/eid/article/28/7/22-0526_article)

To detect new and changing SARS-CoV-2 variants, we investigated candidate Delta-Omicron recombinant genomes from Centers for Disease Control and Prevention national genomic surveillance. Laboratory and bioinformatic investigations identified and validated 9 genetically related SARS-CoV-2 viruses with a hybrid Delta-Omicron spike protein.

   [https://wwwnc.cdc.gov/eid/article/28/7/22-0428_article](https://wwwnc.cdc.gov/eid/article/28/7/22-0428_article)

As of April 2022, the Omicron BA.1 variant of concern of SARS-CoV-2 was spreading quickly around the world and outcompeting other circulating strains. We examined its stability on various surfaces and found that this Omicron variant is more stable than its ancestral strain on smooth and porous surfaces.

   [https://www.nature.com/articles/s41586-022-04856-1](https://www.nature.com/articles/s41586-022-04856-1)

Here, we evaluated the replicative ability and pathogenicity of authentic infectious BA.2 isolates in immunocompetent and human ACE2 (hACE2)-expressing mice and hamsters. In contrast to recent data with chimeric, recombinant SARS-CoV-2 strains expressing the spike proteins of BA.1 and BA.2 on an ancestral WK-521 backbone, we observed similar infectivity and pathogenicity in mice and hamsters between BA.2 and BA.1, and less pathogenicity compared to early SARS-CoV-2 strains. We also observed a marked and significant reduction in the neutralizing activity of plasma from COVID-19 convalescent individuals and vaccine recipients against BA.2 compared to ancestral and Delta variant strains. In addition, we found that some therapeutic monoclonal antibodies (REGN10987/REGN10933, COV2-2196/COV2-2130, and S309) and antiviral drugs (molnupiravir, nirmatrelvir, and S-217622) can restrict viral infection in the respiratory organs of BA.2-infected hamsters. These findings suggest that the replication and pathogenicity of BA.2 is comparable to that of BA.1 in rodents and that several
therapeutic monoclonal antibodies and antiviral compounds are effective against Omicron/BA.2 variants.

**Clinical Syndrome**


Risks of venous thromboembolism and arterial thromboembolism were up to 1% among COVID-19 cases, and increased with age, among males, and in those who were hospitalised. Their occurrence was associated with excess mortality, underlying the importance of developing effective treatment strategies that reduce their frequency.

**Diagnostics & Screening**


Among the 6 selected models, those based only on symptoms and/or risk exposure were found to be less efficient than those based on biological parameters and/or radiological examination with smallest AUROC values (< 0.80). Although quite acceptable and similar results were found between all models, the importance of radiological examination was also emphasized, making it difficult to find an appropriate triage system to classify patients at risk for COVID-19.


With the rapid wave of Omicron (B.1.1.529) SARS-CoV-2 cases detected worldwide and the significant mutation profile of this Variant of Concern (VOC), questions have been raised about its impact on SARS-CoV-2 tissue tropism and viral load. As Omicron more adeptly replicates in the upper respiratory tract than previous variants, it has been proposed that saliva or oral specimens may detect Omicron with greater sensitivity than those from the nasopharynx, although evidence for this to date has not included evaluation of nasopharyngeal swabs (NPS). Diagnostic testing recommendations which maximize analytical sensitivity are particularly crucial for patients who may qualify for treatment with monoclonal antibodies and/or antivirals.

**Epidemiology & Public Health**

7. **Who was at risk for COVID-19 late in the US pandemic? Insights from a population health machine learning model.** Adeoye EA, Rozenfeld Y, Beam J, Boudreau K, Cox EJ, Scanlan JM.
Patient records were extracted for all COVID-19 nasal swab PCR tests performed within the Providence St. Joseph Health system from February to October of 2020. A total of 316,599 participants were included in this study, and approximately 7.7% (n = 24,358) tested positive for COVID-19. A gradient boosting model, LightGBM (LGBM), predicted risk of initial infection with an area under the receiver operating characteristic curve of 0.819. Factors that predicted infection were cough, fever, being a member of the Hispanic or Latino community, being Spanish speaking, having a history of diabetes or dementia, and living in a neighborhood with housing insecurity. A model trained on sociodemographic, environmental, and medical history data performed well in predicting risk of a positive COVID-19 test.


Here we describe co-infection with the SARS-CoV-2 variants of concern Omicron and Delta in two epidemiologically unrelated adult patients with chronic kidney disease requiring maintenance haemodialysis. Both variants were co-circulating in the community at the time of detection. Genomic surveillance based on amplicon- and probe-based sequencing using short- and long-read technologies identified and quantified subpopulations of Delta and Omicron viruses in respiratory samples. These findings highlight the importance of integrated genomic surveillance in vulnerable populations and provide diagnostic pathways to recognise SARS-CoV-2 co-infection using genomic data.

**Prognosis**


We derived and validated a simple bedside tool for predicting hospital mortality for patients with COVID-19 being considered for ECMO, and compared its performance to the performance of the Respiratory ECMO Survival Prediction (RESP) score, a commonly used prognostic model for survival during ECMO developed prior to the COVID-19 pandemic.

**Survivorship & Rehabilitation**


Regardless of initial disease severity, COVID-19 survivors had longitudinal improvements in physical and mental health, with most returning to their original work within 2 years; however, the burden of symptomatic sequelae remained fairly high. COVID-19 survivors had a remarkably lower health status than the general population at 2 years. The study findings indicate that there is an urgent need to explore the pathogenesis of long COVID and develop effective interventions to reduce the risk of long COVID.

We performed a population-based, nationwide study of cumulative incidence, risk factors and clinical course of long-term oxygen therapy (LTOT) after COVID-19, using data from the SCIFI-PEARL study (2). We included all people in Sweden aged ≥16 years with a laboratory confirmed SARS-CoV-2 infection from 1st January 2020 until 31st August 2021, with no LTOT before the COVID-19 diagnosis.

**Therapeutics**


In patients with acute hypoxemic respiratory failure from COVID-19, prone positioning, compared with usual care without prone positioning, did not significantly reduce endotracheal intubation at 30 days. However, the effect size for the primary study outcome was imprecise and does not exclude a clinically important benefit.


We aimed to assess whether CP administered during the first week of symptoms reduced the disease progression or risk of hospitalization of outpatients. Two multicenter, double-blind randomized trials (NCT04621123, NCT04589949) were merged with data pooling starting when <20% of recruitment target was achieved. A Bayesian-adaptive individual patient data meta-analysis was implemented. Outpatients aged ≥50 years and symptomatic for ≤7 days were included. The intervention consisted of 200-300mL of CP with a predefined minimum level of antibodies. Primary endpoints were a 5-point disease severity scale and a composite of hospitalization or death by 28 days. Amongst the 797 patients included, 390 received CP and 392 placebo; they had a median age of 58 years, 1 comorbidity, 5 days symptoms and 93% had negative IgG antibody-test. Seventy-four patients were hospitalized, 6 required mechanical ventilation and 3 died. The odds ratio (OR) of CP for improved disease severity scale was 0.936 (credible interval (CI) 0.667-1.311); OR for hospitalization or death was 0.919 (CI 0.592-1.416). CP effect on hospital admission or death was largest in patients with ≤5 days of symptoms (OR 0.658, 95%CI 0.394-1.085). CP did not decrease the time to full symptom resolution.


Of 10,036 patients with SARS-CoV-2 infection, 522 receiving sotrovimab were matched to 1,563 not receiving mAbs. Compared to mAb-untreated patients, sotrovimab treatment was associated with a 63% decrease in the odds of all-cause hospitalization (raw rate 2.1% versus 5.7%; adjusted OR 0.37,
95% CI 0.19-0.66) and an 89% decrease in the odds of all-cause 28-day mortality (raw rate 0% versus 1.0%; adjusted OR 0.11, 95% CI 0.0-0.79), and may reduce respiratory disease severity among those hospitalized. Real-world evidence demonstrated sotrovimab effectiveness in reducing hospitalization and all-cause 28-day mortality among COVID-19 outpatients during the Delta variant phase.


Among patients with COVID-19 pneumonia and mild hypoxaemia, the use of HFNO did not significantly reduce the likelihood of escalation of respiratory support.


Clazakizumab significantly improved 28-day ventilator-free survival, 28- and 60-day overall survival, as well as clinical outcomes in hospitalized patients with COVID-19 and hyperinflammation.


Raloxifene showed evidence of effect in the primary virologic endpoint in the treatment of early mild to moderate COVID-19 patients shortening the time of viral shedding. The safety profile was consistent with that reported for other indications. Raloxifene may represent a promising pharmacological option to prevent or mitigate COVID-19 disease progression.

**Transmission / Infection Control**


Administration of high-titer CCP as post-exposure prophylaxis, while appearing safe, did not prevent SARS-CoV-2 infection.

**Vaccines / Immunology**

19. **Safety, immunogenicity, and reactogenicity of BNT162b2 and mRNA-1273 COVID-19 vaccines given as fourth-dose boosters following two doses of ChAdOx1 nCoV-19 or BNT162b2 and a third dose of BNT162b2 (COV-BOOST): a multicentre, blinded, phase 2, randomised trial.** Munro APS et al. *Lancet Infect Dis.* 2022 May 9:S1473-3099(22)00271-7. doi: 10.1016/S1473-
Fourth-dose COVID-19 mRNA booster vaccines are well tolerated and boost cellular and humoral immunity. Peak responses after the fourth dose were similar to, and possibly better than, peak responses after the third dose.


To assess the severity of COVID-19 due to Omicron in Ontario LTC residents, we undertook a chart review of the first 100 residents of Ontario LTC homes owned or managed by Extendicare Ltd. who were diagnosed with COVID-19 after December 15, 2021.


In a period largely pre-dating Omicron variant circulation, effectiveness of two mRNA doses against COVID-19-associated hospitalization was largely sustained through 9 months.

22. **Trajectory of long covid symptoms after covid-19 vaccination: community based cohort study.** Ayoubkhani D, et al. *BMJ.* 2022 May 18;377:e069676. doi: 10.1136/bmj-2021-069676. [https://doi.org/10.1136/bmj-2021-069676](https://doi.org/10.1136/bmj-2021-069676)

The likelihood of long covid symptoms was observed to decrease after covid-19 vaccination and evidence suggested sustained improvement after a second dose, at least over the median follow-up of 67 days. Vaccination may contribute to a reduction in the population health burden of long covid, although longer follow-up is needed.

23. **Limited cross-variant immunity from SARS-CoV-2 Omicron without vaccination.** Suryawanshi RK, et al. *Nature.* 2022 May 18. doi: 10.1038/s41586-022-04865-0. [https://doi.org/10.1038/s41586-022-04865-0](https://doi.org/10.1038/s41586-022-04865-0)

Here we show that without vaccination, infection with Omicron induces a limited humoral immune response in mice and humans. Sera from mice overexpressing the human ACE2 receptor and infected with Omicron neutralize only Omicron, but no other VOCs, whereas broader cross-variant neutralization was observed after WA1 and Delta infections. Unlike WA1 and Delta, Omicron replicates to low levels in the lungs and brains of infected animals, leading to mild disease with reduced pro-inflammatory cytokine expression and diminished activation of lung-resident T cells. Sera from unvaccinated, Omicron-infected individuals show the same limited neutralization of only Omicron itself. In contrast, Omicron breakthrough infections induce overall higher neutralization titers against all VOCs. Our results demonstrate that Omicron infection enhances preexisting immunity elicited by vaccines but, on its own, may not confer broad protection against non-Omicron variants in unvaccinated individuals.
Results indicate that BA.3 is not a substantial immune-escape variant, a finding that is likely due to its reduced number of mutations in the receptor-binding domain as compared with the BA.1 and BA.2 variants. However, the deltacron variant retains the strong resistance of other omicron sublineages and has no enhanced sensitivity to serum obtained during the delta wave. Although the effect of the delta-derived spike mutations in the N-terminal domain on virus replication and pathogenesis remains unclear, these mutations do not appear to impair neutralization resistance. Recombination of SARS-CoV-2 variants and the potential emergence of a more virulent variant with strong immune escape remains a critical concern and requires ongoing monitoring.

The two SARS-CoV-2 mRNA vaccines could be used with flexibility for the second dose of COVID-19 primo vaccination. Tolerance remains good regardless of vaccine sequence although mRNA-1273 was more reactogenic.

**Women & Children**

Safety findings for BNT-162b2 vaccine from 3 US monitoring systems in children ages 5-11 years show that most reported adverse events were mild and no safety signals were observed in active surveillance. VAERS reporting rates of myocarditis after dose 2 in this age group were substantially lower than those observed among adolescents ages 12-15 years.

Despite recent endorsement from official and professional bodies, unequivocally recommending COVID-19 vaccination, hesitancy among pregnant persons remains high. The accumulated evidence clearly demonstrates that pregnant persons are a special risk group for COVID-19, with increased risk of intensive care unit admission, extracorporeal membranous oxygenation requirement, preterm birth and perinatal death. These risks are further increased with some variants of concern, and vaccination of pregnant persons reduces the COVID related increase in maternal or fetal morbidity. Data from over 180,000 vaccinated show immunization against COVID-19 with an mRNA vaccine is safe for pregnant persons. Many observational studies comparing perinatal outcomes between vaccinated and unvaccinated pregnant persons have had reassuring findings and did not demonstrate detrimental effects on pregnancy or the newborn. Immunization with mRNA vaccines does not increase the risk of miscarriage, preterm delivery, low birth weight, maternal or neonatal intensive care unit admission, fetal death, fetal abnormality or pulmonary embolism. Moreover, observational data corroborate the
findings of randomized trials that mRNA vaccination is highly effective at preventing severe SARS-CoV-2 infection in pregnant persons, emphasizing that the potential maternal and fetal benefits of vaccination greatly outweigh the potential risks of vaccination. Ensuring pregnant persons have unrestricted access to COVID-19 vaccination should be a priority in every country around the globe.


We identified 19 children who had a history of SARS-CoV-2 infection and manifest a variety of CNS inflammatory diseases: encephalopathy, cerebellar ataxia, ADEM, neuromyelitis optica spectrum disorder (NMOSD) or optic neuritis. All patients had a history of SARS-CoV-2 exposure, and all tested positive for circulating antibodies against SARS-CoV-2. At the onset of the neurologic disease, SARS-CoV-2 PCR results (nasopharyngeal swabs) were positive in 8 children. SARS2-CoV-2 represents a new trigger of post infectious CNS inflammatory diseases in children.


Recently, there have been reports of children with a severe acute form of hepatitis in the UK, Europe, the USA, Israel, and Japan. Most patients present with gastrointestinal symptoms and then progress to jaundice and, in some cases, acute liver failure. So far, no common environmental exposures have been found, and an infectious agent remains the most plausible cause. Hepatitis viruses A, B, C, D, and E have not been found in these patients, but 72% of children with severe acute hepatitis in the UK who were tested for an adenovirus had an adenovirus detected, and out of 18 subtyped cases in the UK, all were identified as adenovirus 41F.1, 2 This is not an uncommon subtype, and it predominantly affects young children and immunocompromised patients. However, to our knowledge, adenovirus 41F has not previously been reported to cause severe acute hepatitis.


The European Medicines Agency has initiated an assessment of menstrual disturbance after COVID-19 vaccination. However, according to current knowledge, any changes in the menstrual cycle seem to be short-term and transistent.


Gestational diabetes mellitus, combined with periconceptional overweight/obesity, is independently associated with severe maternal course of COVID-19, especially when the mothers require insulin and COVID-19 is diagnosed with or after gestational diabetes mellitus diagnosis. These combined factors
exhibited a moderate effect on neonatal outcomes. Women with gestational diabetes mellitus and body mass index >25 kg/m² are a particularly vulnerable group in the case of COVID-19.


This study suggests that MIS-C during the Omicron wave was less severe than during the Alpha or Delta waves of the COVID-19 pandemic. Possible explanations include the Omicron variant itself, previous infection with SARS-CoV-2, vaccination against SARS-CoV-2, and improvement in treatment over time. In addition, the incidence rate of MIS-C during the Omicron wave was lower than during the Delta and Alpha waves. A 2022 study from South Africa on the Omicron wave reported no cases of MIS-C, a finding that corroborates these results.


Myopericarditis is a severe adverse event to COVID-19 vaccines. The highest risk has been reported in males aged 12-29 years. According to the US Vaccine Adverse Event Reporting System (VAERS), the risk in children aged 5-11 years is low with 11 reported cases following 8.7 million doses of Pfizer-BioNTech vaccine. However, these numbers may be underestimated due to underreporting.

**GUIDELINES & CONSENSUS STATEMENTS**


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

*CDC recommends Pfizer COVID boosters for kids ages 5 to 11*
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