Providence

COVID-19 Resource Desk

#97 | 3.6.2022 to 3.12.2022

Prepared by System Library Services Retraction Watch

New Research

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

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

Epidemiology & Public Health

1. **Quantifying the effects of the COVID-19 pandemic on gender equality on health, social, and economic indicators: a comprehensive review of data from March, 2020, to September, 2021.** Flor LS et al. *Lancet.* 2022 Mar 2:S0140-6736(22)00008-3. doi: 10.1016/S0140-6736(22)00008-3. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00008-3/fulltext

The most significant gender gaps identified in our study show intensified levels of pre-existing widespread inequalities between women and men during the COVID-19 pandemic. Political and social leaders should prioritise policies that enable and encourage women to participate in the labour force and continue their education, thereby equipping and enabling them with greater ability to overcome the barriers they face.

2. **Secondary Attack Rates for Omicron and Delta Variants of SARS-CoV-2 in Norwegian Households.** Jørgensen SB, Nygård K, Kacelnik O, Telle K. *JAMA.* 2022 Mar 7. doi: 10.1001/jama.2022.3780. https://jamanetwork.com/journals/jama/fullarticle/2789920

Secondary attack rate was 25.1% when the variant of the index case was Omicron, 19.4% when it was Delta, and 17.9% when it was nonclassified . Odds ratios were higher for men, unvaccinated individuals, and those older than 30 years.

3. **Rapid spread of SARS-CoV-2 Omicron subvariant BA.2 in a single-source community outbreak.** Cheng VC et al. *Clin Infect Dis*. 2022 Mar 10:ciac203. doi: 10.1093/cid/ciac203. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac203/6546687

Our study highlights the exceptionally high transmissibility of the Omicron variant BA.2 sublineage in Hong Kong where stringent measures are implemented as part of the elimination strategy. Continual genomic surveillance is crucial in monitoring the emergence of epidemiologically important Omicron sub-variants.

4. **COVID-19 Vaccine Provider Access and Vaccination Coverage Among Children Aged 5-11 Years - United States, November 2021-January 2022.** Kim C et al. *MMWR Morb Mortal Wkly Rep*. 2022 Mar 11;71(10):378-383. doi: 10.15585/mmwr.mm7110a4. https://www.cdc.gov/mmwr/volumes/71/wr/mm7110a4.htm?s_cid=mm7110a4_w

As of January 18, 2022 (11 weeks after program launch), 39,786 providers had administered 13.3 million doses. First dose coverage at 4 weeks after launch was 15.0%, and at 11 weeks was 27.7%. Overall series completion at 11 weeks after launch was 19.1%. Pharmacies administered 46.4% of doses to this age group, including 48.7% of doses in high SVI areas and 44.4% in low SVI areas. Although COVID-19 vaccination coverage rates were low, particularly in high SVI areas, first dose coverage improved over time. Additional outreach is critical, especially in high SVI areas, to improve vaccine confidence and increase coverage rates among children aged 5-11 years.

Survivorship & Rehabilitation

5. **Long-term health-related quality of life in non-hospitalised COVID-19 cases with confirmed SARS-CoV-2 infection in England: Longitudinal analysis and cross-sectional comparison with controls.** Sandmann FG et al. *Clin Infect Dis*. 2022 Mar 5:ciac151. doi: 10.1093/cid/ciac151. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac151/6542727

One in 6 cases report ongoing symptoms at 6 months, and 10% report prolonged loss of function compared to pre-COVID-19 baselines. A marked health burden was observed among older COVID-19 cases and those with persistent physical symptoms.

6. **SARS-CoV-2 is associated with changes in brain structure in UK Biobank.** Douaud G et al. *Nature.* 2022 Mar 7. doi: 10.1038/s41586-022-04569-5. https://www.nature.com/articles/s41586-022-04569-5

Here, we investigated brain changes in 785 UK Biobank participants (aged 51-81) imaged twice, including 401 cases who tested positive for infection with SARS-CoV-2 between their two scans, with 141 days on average separating their diagnosis and second scan, and 384 controls. The availability of pre-infection imaging data reduces the likelihood of pre-existing risk factors being misinterpreted as disease effects. We identified significant longitudinal effects when comparing the two groups, including: (i) greater reduction in grey matter thickness and tissue-contrast in the orbitofrontal cortex and parahippocampal gyrus, (ii) greater changes in markers of tissue damage in regions functionally-connected to the primary olfactory cortex, and (iii) greater reduction in global brain size. The infected participants also showed on average larger cognitive decline between the two timepoints. Importantly, these imaging and cognitive longitudinal effects were still seen after excluding the 15 cases who had been hospitalised. These mainly limbic brain imaging results may be the in vivo hallmarks of a degenerative spread of the disease via olfactory pathways, of neuroinflammatory events, or of the loss of sensory input due to anosmia. Whether this deleterious impact can be partially reversed, or whether these effects will persist in the long term, remains to be investigated with additional follow up.

7. **Comparison of 6-Month Outcomes of COVID-19 vs Non-COVID-19 Survivors of Critical Illness.** Hodgson CL et al. *Am J Respir Crit Care Med.* 2022 Mar 8. doi: 10.1164/rccm.202110-2335OC. https://www.atsjournals.org/doi/10.1164/rccm.202110-2335OC

At 6-months there was no difference in new disability for patients requiring mechanical ventilation for acute respiratory failure due to COVID-19 compared to non-COVID-19.

8. **Evaluation of the Post-COVID-19 Functional Status (PCFS) Scale in a cohort of patients recovering from hypoxemic SARS-CoV-2 pneumonia.** Benkalfate N et al. *BMJ Open Respir Res.*

2022 Mar;9(1):e001136. doi: 10.1136/bmjresp-2021-001136. https://bmjopenrespres.bmj.com/content/9/1/e001136

The PCFS Scale seems to be a suitable instrument to screen for patients who will require careful follow-up after COVID-19 hypoxemic pneumonia even in the absence of pulmonary sequelae.

Therapeutics

9. **Anticoagulation in Patients With COVID-19: JACC Review Topic of the Week.** Farkouh ME et al. *J Am Coll Cardiol.* 2022 Mar 8;79(9):917-928. doi: 10.1016/j.jacc.2021.12.023. https://www.sciencedirect.com/science/article/pii/S0735109722000079

Observational studies and randomized trials have investigated whether full-dose anticoagulation may improve outcomes compared with prophylactic dose heparin. Although no benefit for therapeutic heparin has been found in patients who are critically ill hospitalized with COVID-19, some studies support a possible role for therapeutic anticoagulation in patients not yet requiring intensive care unit support. We summarize the pathology, rationale, and current evidence for use of anticoagulation in patients with COVID-19 and describe the main design elements of the ongoing FREEDOM COVID-19 Anticoagulation trial, in which 3,600 hospitalized patients with COVID-19 not requiring intensive care unit level of care are being randomized to prophylactic-dose enoxaparin vs therapeutic-dose enoxaparin vs therapeutic-dose apixaban.

10. **Early administration of tocilizumab in hospitalized COVID-19 patients with elevated inflammatory markers; COVIDSTORM - A prospective, randomized, single center, open label study.** Broman N et al. *Clin Microbiol Infect.* 2022 Mar 5:S1198-743X(22)00104-5. doi: 10.1016/j.cmi.2022.02.027. https://www.sciencedirect.com/science/article/pii/S1198743X22001045

In hospitalized COVID-19 patients with hypoxemia and elevated inflammation markers, administration of tocilizumab in addition to standard of care was associated with significantly better clinical recovery by day 28 and a shorter hospitalization compared to standard of care alone.

11. **Association Between Dexamethasone Treatment After Hospital Discharge for Patients With COVID-19 Infection and Rates of Hospital Readmission and Mortality.** Huang CW, et al. *JAMA Netw Open.* 2022 Mar 1;5(3):e221455. doi: 10.1001/jamanetworkopen.2022.1455. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2789710

In this cohort study of patients with COVID-19, continuing treatment with dexamethasone, 6 mg/d, at discharge was not associated with a reduction in 14-day all-cause readmission or mortality. This finding suggests that dexamethasone should not be routinely prescribed beyond discharge for individuals with COVID-19.

12. **Efficacy of Antiviral Agents against the SARS-CoV-2 Omicron Subvariant BA.2.** Takashita E et al. *N Engl J Med.* 2022 Mar 9. doi: 10.1056/NEJMc2201933. https://www.nejm.org/doi/10.1056/NEJMc2201933

The susceptibilities of omicron/BA.2 to remdesivir, molnupiravir, and nirmatrelvir were similar to those of the ancestral strain and other variants of concern. Clinical studies are warranted to determine whether these antiviral therapies are indeed effective against omicron/BA.2 infections. Our data

indicate that some therapeutic monoclonal antibodies (REGN10987–REGN10933, COV2-2196–COV2-2130, and S309) have lower neutralizing activity against omicron/BA.2 than against earlier variant strains.

13. **Resistance Mutations in SARS-CoV-2 Delta Variant after Sotrovimab Use.** Rockett R et al. *N Engl J Med.* 2022 Mar 9. doi: 10.1056/NEJMc2120219. https://www.nejm.org/doi/10.1056/NEJMc2120219

Data show the persistence of viable SARS-CoV-2 in patients after sotrovimab infusions and the rapid development of spike gene mutations associated with high-level sotrovimab resistance in vitro. These findings underscore the importance of stewardship of monoclonal antibodies, particularly because sotrovimab is one of the few monoclonal antibodies with retained activity against the B.1.1.529 (omicron) variant.

Transmission / Infection Control

14. **School Masking Policies and Secondary SARS-CoV-2 Transmission.** Boutzoukas AE et al. *Pediatrics.* 2022 Mar 9. doi: 10.1542/peds.2022-056687. https://publications.aap.org/pediatrics/article/doi/10.1542/peds.2022-056687/185379/School-Masking-Policies-and-Secondary-SARS-CoV-2

1,112,899 students and 157,069 staff attended 61 K-12 districts across 9 states that met inclusion criteria. The districts reported 40,601 primary and 3,085 secondary infections. Six districts had optional masking policies, 9 had partial masking policies, and 46 had universal masking. Districts that optionally masked throughout the study period had 3.6 times the rate of secondary transmission as universally masked districts. For every 100 community-acquired cases, universally masked districts had 7.3 predicted secondary infections, while optionally masked districts had 26.4. Secondary transmission across the cohort was modest (<10% of total infections) and universal masking was associated with reduced secondary transmission compared to optional masking.

15. **SARS-CoV-2 Incidence in K-12 School Districts with Mask-Required Versus Mask-Optional Policies - Arkansas, August-October 2021.** Donovan CV et al. *MMWR Morb Mortal Wkly Rep.* 2022 Mar 11;71(10):384-389. doi: 10.15585/mmwr.mm7110e1. https://www.cdc.gov/mmwr/volumes/71/wr/mm7110e1.htm?s_cid=mm7110e1_w

Observed-to-expected ratios for full and partial mask policies were lower than ratios for districts with no mask policy but were slightly higher for districts with partial policies than for those with full mask policies. Among districts that switched from no mask requirement to any mask requirement (full or partial), incidence among students and staff members decreased by 479.7 per 100,000 (p<0.01) upon implementation of the mask policy. In areas with high COVID-19 community levels, masks are an important part of a multicomponent prevention strategy in K-12 settings (5).

Vaccines / Immunology

16. **Covid-19 Vaccine Effectiveness against the Omicron (B.1.1.529) Variant.** Andrews N et al. *N Engl J Med.* 2022 Mar 2. doi: 10.1056/NEJMoa2119451. https://www.nejm.org/doi/10.1056/NEJMoa2119451

Primary immunization with two doses of ChAdOx1 nCoV-19 or BNT162b2 vaccine provided limited protection against symptomatic disease caused by the omicron variant. A BNT162b2 or mRNA-1273 booster after either the ChAdOx1 nCoV-19 or BNT162b2 primary course substantially increased protection, but that protection waned over time.

17. **Real-world incidence of breakthrough COVID-19 hospitalization after vaccination versus natural infection in a large, local, empaneled primary care population using time-to-event analysis.** Pollock BD, et al. *Clin Infect Dis.* 2022 Mar 5:ciac186. doi: 10.1093/cid/ciac186. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac186/6542971

We followed 106,349 primary care patients for 22,385,309 person-days across 21 calendar months. There were 69 breakthrough COVID-19 hospitalizations: 65/102,613(0.06%) among fully vaccinated, 3/11,047(0.03%) among those previously infected, and 1/7,313(0.01%) among those with both statuses. This data gives primary care providers real-world context regarding breakthrough COVID-19 hospitalization risk.

18. **Waning of SARS-CoV-2 booster viral-load reduction effectiveness.** Levine-Tiefenbrun M, et al. *Nat Commun.* 2022 Mar 4;13(1):1237. doi: 10.1038/s41467-022-28936-y. https://www.nature.com/articles/s41467-022-28936-y

The BNT162b2 COVID-19 vaccine has been shown to reduce viral load of breakthrough infections (BTIs), an important factor affecting infectiousness. This viral-load protective effect has been waning with time post the second vaccine and later restored with a booster shot. It is currently unclear though for how long this regained effectiveness lasts. Analyzing Ct values of SARS-CoV-2 qRT-PCR tests of over 22,000 infections during a Delta-variant-dominant period in Israel, we find that this viral-load reduction effectiveness significantly declines within months post the booster dose. Adjusting for age, sex and calendric date, Ct values of RdRp gene initially increases by 2.7 [CI: 2.3-3.0] relative to unvaccinated in the first month post the booster dose, yet then decays to a difference of 1.3 [CI: 0.7-1.9] in the second month and becomes small and insignificant in the third to fourth months. The rate and magnitude of this post-booster decline in viral-load reduction effectiveness mirror those observed post the second vaccine. These results suggest rapid waning of the booster's effectiveness in reducing infectiousness, possibly affecting community-level spread of the virus.

19. **Vaccine Effectiveness of Three vs. Two Doses of SARS-CoV-2 mRNA Vaccines in a High Risk National Population.** Butt AA, et al. *Clin Infect Dis.* 2022 Mar 4:ciac178. doi: 10.1093/cid/ciac178. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac178/6542712

Third dose of a SARS-CoV-2 mRNA vaccine is associated with high VE against symptomatic infection, hospitalization, and critical disease in the pre-Omicron era.

20. **Immune response to SARS-CoV-2 after a booster of mRNA-1273: an open-label phase 2 trial.** Chu L et al. *Nat Med.* 2022 Mar 3. doi: 10.1038/s41591-022-01739-w. https://www.nature.com/articles/s41591-022-01739-w

Results show that a booster injection of mRNA-1273 more than 6 months after completing the primary two-dose series is safe and elicited nAb titers that were statistically significantly higher than the peak

titers detected after the primary vaccination series, suggesting that a booster dose of mRNA-1273 might result in increased vaccine effectiveness against infection and disease caused by SARS-CoV-2.

21. **B-cell-responses to vaccination with BNT162b2 and mRNA-1273 six months after second dose.** Markewitz R et al. *Clin Microbiol Infect.* 2022 Mar 5:S1198-743X(22)00105-7. doi: 10.1016/j.cmi.2022.02.028. https://www.sciencedirect.com/science/article/pii/S1198743X22001057

While the clinical consequences of decreasing anti-SARS-CoV-2 antibody titers cannot be estimated with certainty, a lowered degree of clinical protection against SARS-CoV-2 is possible. Persistently stronger responses to mRNA-1273 suggest that it might confer greater protection than BNT162b2, even six months after the second vaccination. Both examined vaccinations do not induce ANA within the examined time frame.

22. **Effect of mRNA Vaccine Boosters against SARS-CoV-2 Omicron Infection in Qatar.** Abu-Raddad LJ et al. *N Engl J Med.* 2022 Mar 9. doi: 10.1056/NEJMoa2200797. https://www.nejm.org/doi/10.1056/NEJMoa2200797

The messenger RNA (mRNA) boosters were highly effective against symptomatic delta infection, but they were less effective against symptomatic omicron infection. However, with both variants, mRNA boosters led to strong protection against Covid-19-related hospitalization and death.

23. **Comparison of Seroconversion in Children and Adults with Mild COVID-19.** Toh ZQ et al. *JAMA Netw Open.* 2022 Mar 1;5(3):e221313. doi: 10.1001/jamanetworkopen.2022.1313. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2789845

The findings of this cohort study suggest that among patients with mild COVID-19, children may be less likely to have seroconversion than adults despite similar viral loads. This finding has implications for future protection after SARS-CoV-2 infection in children and for interpretation of serosurveys that involve children. Further research to understand why seroconversion and development of symptoms are potentially less likely in children after SARS-CoV-2 infection and to compare vaccine responses may be of clinical and scientific importance.

24. **Comparison of Moderna versus Pfizer-BioNTech COVID-19 vaccine outcomes: A target trial emulation study in the U.S. Veterans Affairs healthcare system.** Ioannou GN, et al. *EClinicalMedicine.* 2022 Mar 5;45:101326. doi: 10.1016/j.eclinm.2022.101326. eCollection 2022 Mar. https://www.sciencedirect.com/science/article/pii/S2589537022000566

In conclusion, although absolute rates of infection, hospitalization and death in both vaccine groups were low regardless of the vaccine received, our data suggests that compared to BNT162b2, vaccination with mRNA-1273 resulted in significantly lower rates of SARS-CoV-2-infection and SARS-CoV-2-related hospitalization. These differences were greater with longer follow-up time since vaccination and even more pronounced in the Delta variant era.

25. **Safety of mRNA vaccines administered during the initial 6 months of the US COVID-19 vaccination programme: an observational study of reports to the Vaccine Adverse Event Reporting System and v-safe.** Rosenblum HG et al. *Lancet Infect Dis.* 2022 Mar 7:S1473-

3099(22)00054-8. doi: 10.1016/S1473-3099(22)00054-8. https://www.sciencedirect.com/science/article/pii/S1473309922000548

Safety data from more than 298 million doses of mRNA COVID-19 vaccine administered in the first 6 months of the US vaccination programme show that most reported adverse events were mild and short in duration.

26. **Interim Estimates of 2021-22 Seasonal Influenza Vaccine Effectiveness - United States, February 2022.** Chung JR et al. *MMWR Morb Mortal Wkly Rep.* 2022 Mar 11;71(10):365-370. doi: 10.15585/mmwr.mm7110a1. https://www.cdc.gov/mmwr/volumes/71/wr/mm7110a1.htm?s_cid=mm7110a1_w

This analysis indicates that influenza vaccination did not reduce the risk for outpatient medically attended illness with influenza A(H3N2) viruses that predominated so far this season. Enrollment was insufficient to generate reliable VE estimates by age group or by type of influenza vaccine product (1). CDC recommends influenza antiviral medications as an adjunct to vaccination; the potential public health benefit of antiviral medications is magnified in the context of reduced influenza VE. CDC routinely recommends that health care providers continue to administer influenza vaccine to persons aged ≥6 months as long as influenza viruses are circulating, even when VE against one virus is reduced, because vaccine can prevent serious outcomes (e.g., hospitalization, intensive care unit (ICU) admission, or death) that are associated with influenza A(H3N2) virus infection and might protect against other influenza viruses that could circulate later in the season.

27. **Clinical severity of, and effectiveness of mRNA vaccines against, covid-19 from omicron, delta, and alpha SARS-CoV-2 variants in the United States: prospective observational study.** Lauring AS et al. *BMJ.* 2022 Mar 9;376:e069761. doi: 10.1136/bmj-2021-069761. https://www.bmj.com/content/376/bmj-2021-069761

mRNA vaccines were found to be highly effective in preventing covid-19 associated hospital admissions related to the alpha, delta, and omicron variants, but three vaccine doses were required to achieve protection against omicron similar to the protection that two doses provided against the delta and alpha variants. Among adults admitted to hospital with covid-19, the omicron variant was associated with less severe disease than the delta variant but still resulted in substantial morbidity and mortality. Vaccinated patients admitted to hospital with covid-19 had significantly lower disease severity than unvaccinated patients for all the variants.

Women & Children

28. **Extracorporeal membrane oxygenation in children with COVID-19 and PIMS-TS during the second and third wave.** EuroECMO neonatal and paediatric COVID-19 Working Group and EuroELSO Steering Committee. *Lancet Child Adolesc Health*. 2022 Mar 3:S2352-4642(22)00065-7. doi: 10.1016/S2352-4642(22)00065-7. https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(22)00065-7/fulltext

We found that the use of ECMO in children with COVID-19 in Europe is still low, but survival after hospital discharge increased compared with the first wave (96% in the second and third waves vs 57% in the first wave), which might be explained by a better patient selection and understanding of the management of critical illness in children with COVID-19. Patients with PIMS-TS had a higher

inflammatory profile compared with patients with ARDS, and children with COVID-19 critical illness had a higher rate of ECMO survival to hospital discharge than adults (96% in children vs 55% in adults).

29. **Age-related changes in the nasopharyngeal microbiome are associated with SARS-CoV-2 infection and symptoms among children, adolescents, and young adults.** Hurst JH et al. *Clin Infect Dis*. 2022 Mar 5:ciac184. doi: 10.1093/cid/ciac184. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac184/6542968

We identified interactive relationships between age and specific nasopharyngeal microbiome features that are associated with SARS-CoV-2 infection susceptibility and symptoms in children, adolescents, and young adults. Our data suggest that the upper respiratory microbiome may be a mechanism by which age influences SARS-CoV-2 susceptibility and illness severity.

30. **COVID-19-Associated Croup in Children.** Brewster RCL, et al. *Pediatrics.* 2022 Mar 8. doi: 10.1542/peds.2022-056492. https://publications.aap.org/pediatrics/article/doi/10.1542/peds.2022-056492/185378/COVID-19-Associated-Croup-in-Children

This retrospective analysis of a freestanding children's hospital found that the incidence of croup co-occurring with SARS-CoV-2 infection sharply increased in December 2021, strongly correlating with emergence of the Omicron variant. Other spikes in COVID-19 were not associated with increased diagnoses of croup. Interestingly, the observed rates of hospitalization and re-dosing of croup-directed therapies may indicate a more severe phenotype compared to other viral etiologies. Taken together, our preliminary findings lend compelling evidence to the hypothesis that the Omicron variant causes laryngotracheobronchitis. This tropism shift may stem from differences in protein expression between cells of the lower respiratory versus upper respiratory tract, although variant-specific mechanistic studies remain an active research area.
