2019-nCoV Literature Situation Report (Lit Rep)

June 14, 2021

The scientific literature on COVID-19 is rapidly evolving and these articles were selected for review based on their relevance to Washington State decision making around COVID-19 response efforts. Included in these Lit Reps are some manuscripts that have been made available online as pre-prints but have not yet undergone peer review. Please be aware of this when reviewing articles included in the Lit Reps.

Key Takeaways

- **A modeling study found that the approach to distribution of SARS-CoV-2 vaccines between February 19 and Match 17, 2021 in the US may have created "vaccine deserts", defined as areas with localized, geographic barriers to vaccine-associated herd immunity, which the authors suggest may affect population-wide efforts to curb SARS-CoV-2 transmission.** More
- **SARS-CoV-2 RNA levels were significantly higher in symptomatic individuals compared to asymptomatic individuals, and no significant differences in RNA levels were found between adults and children, according to results from a community-based cross-sectional study in King County, Washington.** More
- **A study of SARS-CoV-2 vaccination in Israel found that for every 20 percentage point increase in vaccination coverage there was a 2-fold reduction in the positive test fraction among those in the population who were unvaccinated, which the authors suggest indicates that vaccination provided indirect protection to unvaccinated individuals.** More

Testing and Treatment

- A study conducted between March and July 2020 that assessed the association between COVID-19 mortality and different treatment combinations found that anticoagulation treatment alone was associated with significantly reduced mortality for both patients receiving intensive care and non-intensive care. The four treatment combinations studied were anticoagulation only (OR=0.2), anticoagulation and remdesivir (OR=0.3), anticoagulation and corticosteroids (OR=0.5), and anticoagulation, corticosteroids and remdesivir (OR=0.4). After adjusting for demographic characteristics, clinical characteristics, and all treatment combinations, there was an absolute decrease in the mortality rate by 2.5% between early and late periods of the study.

  Coppock et al. (2021). COVID-19 Treatment Combinations and Associations with Mortality in a Large Multi-Site Healthcare System. PloS One. https://doi.org/10.1371/journal.pone.0252591

- A study comparing the Abbott SARS-CoV-2 nucleocapsid IgG, Beckman-Coulter SARS-CoV-2 spike IgG, and Roche Anti-SARS-CoV-2 nucleocapsid total antibody assays found that all three demonstrated 100% specificity, and sensitivities of 98%, 93%, and 90%, respectively. After the exclusion of samples from immunocompromised patients, all assays exhibited ≥95% sensitivity. In sequential samples collected from the same individuals, the Roche nucleocapsid antibody assay showed continually increasing signal intensity, with maximal values observed at the last time point

examined, while the Beckman spike IgG antibody signal peaked between 14-28 days post-positive SARS-CoV-2 PCR test and steadily declined in subsequent samples.

Poore et al. (June 2021). A Comparison of SARS-CoV-2 Nucleocapsid and Spike Antibody Detection Using Three Commercially Available Automated Immunoassays. Clinical Biochemistry. https://doi.org/10.1016/j.clinbiochem.2021.05.011

Vaccines and Immunity

- *[Pre-print, not peer-reviewed]* As part of the Phase 3 randomized trial for the Novavax SARS-CoV-2 vaccine, a sub-study found that co-administration of an influenza vaccine resulted in no change in influenza vaccine immune response, and a slight reduction in antibody responses to the Novavax vaccine. The authors suggest that this could indicate the viability of combined vaccinations. SARS-CoV-2 vaccine efficacy in this sub-study was 87.5% compared to an efficacy in the main study of 89.8%.

  Heath et al. (June 13, 2021). Safety Immunogenicity and Efficacy of a COVID-19 Vaccine (NVX-CoV2373) Co-Administered With Seasonal Influenza Vaccines. Pre-print downloaded Jun 14 from https://doi.org/10.1101/2021.06.09.21258556

- *[Pre-print, not peer-reviewed]* The presence of SARS-CoV-2 anti-nucleocapsid antibodies at baseline was associated with almost 80% protection against SARS-CoV-2 re-infection for a period of at least eight months, according to a study of healthcare workers (HCW) in Switzerland. Among 4,818 participants, 144 (3%) were seropositive at baseline. Among 2,713 participants with ≥1 SARS-CoV-2 test during follow-up, 3 of 67 (4.5%) seropositive individuals reported a positive result, compared to 547 of 2,646 (20.7%) seronegative participants (RR=0.22).

  Kohler et al. (June 12, 2021). Impact of Baseline SARS-CoV-2 Antibody Status on Syndromic Surveillance and the Risk of Subsequent Covid-19 – a Prospective Multicentre Cohort Study. Pre-print downloaded Jun 14 from https://doi.org/10.1101/2021.06.09.21258422

- A study of SARS-CoV-2 vaccination in 177 different communities in Israel indicated that for every 20 percentage point increase in the proportion of individuals who were vaccinated in a given population, the positive test fraction for the unvaccinated population decreased approximately two-fold, which the authors suggest shows that vaccination provides indirect protection to unvaccinated individuals. Findings from the study indicated that across communities, the positive test fraction in the unvaccinated cohort decreased in proportion to the rate of vaccination in each community.

  Milman et al. (June 2021). Community-Level Evidence for SARS-CoV-2 Vaccine Protection of Unvaccinated Individuals. Nature Medicine. https://doi.org/10.1038/s41591-021-01407-5

- A study of 24 breakthrough SARS-CoV-2 infections among fully vaccinated US Military Health System beneficiaries indicated that most infections (67%) occurred among those without comorbid conditions, 57% reported close contact with a COVID-19 case in the past month, and no case of breakthrough infection resulted in hospitalization. Sequencing from 10 of 13 qPCR-positive specimens indicated the presence of variants of concern or interest including B.1.1.7 (Alpha) (n=2), P.1 (Gamma) (n=1), and B.1.429 (Epsilon) (n=2) in addition to other strains not classified as variants of concern or interest, including B.1.1 (n=1), B.1.1.519 (n=1), B.1.2 (n=2), and B.1.243 (n=1).

  Pollett et al. (June 2021). The SARS-CoV-2 MRNA Vaccine Breakthrough Infection Phenotype Includes Significant Symptoms, Live Virus Shedding, and Viral Genetic Diversity. Clinical Infectious Diseases. https://doi.org/10.1093/cid/ciab543

- Younger age and medical occupation were independent predictors of vaccine hesitancy according to results from a survey of individuals working on a military base in Ohio, administered between November 2020 and January 2021. Among 816 survey respondents, 185 (23%) self-identified as vaccine hesitant. The vaccine hesitant group reported more concern about short-term side effects (43% vs. 26%), long-term side effects (82% vs. 50%), vaccine effectiveness (23% vs. 5%), being infected with COVID-19 from the vaccine (10% vs. 5%), and worry about misinformation/political agenda (43% vs. 31%); these differences were heightened among younger participants. The non-hesitant group was more likely to recommend the COVID-19 vaccine to a friend or family member than the vaccine hesitant group (93% vs. 20%) as were those in the older (≥31 years) age group (79% vs. 67%) and non-medical personnel (81% vs. 52%).

  Theis et al. (June 2021). Perceptions and Concerns Regarding COVID-19 Vaccination in a Military Base Population. Military Medicine. https://doi.org/10.1093/milmed/usab230

Clinical Characteristics and Health Care Setting

- *[Pre-print, not peer-reviewed]* A cohort study of children and adolescents (n=1,501) who were admitted to the hospital between March 18, 2020 and April 30, 2021 in Germany and who tested positive for SARS-CoV-2 found that although approximately half of the cohort was not admitted to the hospital due to COVID-19, 72% had infection-related symptoms during hospitalization. Pre-existing conditions, including respiratory disorders, and neurological, neuromuscular, and cardiovascular diseases, were present in 28% of participants. In a fully adjusted model, patient age, trisomy 21, coinfections and primary immunodeficiencies were significantly associated with intensive care treatment.

  Armann et al. (June 13, 2021). Risk Factors for Hospitalization Disease Severity and Mortality in Children and Adolescents with COVID-19 Results from a Nationwide German Registry. Pre-print downloaded Jun 14 from https://doi.org/10.1101/2021.06.07.21258488

- A cohort study of children and adolescents (n=671) from France, Germany, Spain, Singapore, the UK, and the US found varying trends in COVID-19 hospitalizations and complications between countries, with hospitalizations in the cohort mirroring those of national-level pediatric hospitalization trends for most countries with available data. Laboratory values for 16 assays were analyzed, which indicated elevated levels of inflammatory markers, including C-reactive protein, ferritin, and procalcitonin. Common complications included cardiac arrhythmias (15%), viral pneumonia (13%), and respiratory failure (11%). Few children were treated with COVID-19–directed medications.

  Bourgeois et al. (June 2021). International Analysis of Electronic Health Records of Children and Youth Hospitalized With COVID-19 Infection in 6 Countries. JAMA Network Open. https://doi.org/10.1001/jamanetworkopen.2021.12596

- SARS-CoV-2 RNA levels, as determined by cycle threshold (Ct) values, were significantly higher in symptomatic compared to asymptomatic individuals, and no significant differences in RNA levels were detected between adults and children, according to results from a community-based cross-sectional study in King County, Washington. Among 555 SARS-CoV-2–positive participants, 47 of 123 children (38%) were asymptomatic compared to 31 of 432 (7%) adults, and children with symptoms reported fewer symptoms than symptomatic adults.

  Chung et al. (June 2021). Comparison of Symptoms and RNA Levels in Children and Adults With SARS-CoV-2 Infection in the Community Setting. JAMA Pediatrics. https://doi.org/10.1001/jamapediatrics.2021.2025

Modeling and Prediction

- *[Pre-print, not peer-reviewed]* A modeling study showed that the early SARS-CoV-2 vaccine allocation (February 19 and March 17, 2021) in the US created "vaccine deserts" – areas with localized, geographic barriers to vaccine-associated herd immunity – which the authors suggest may impact population-wide efforts to curb SARS-CoV-2 transmission. Using an empirically-parameterized spatial accessibility model that incorporated high-resolution COVID-19 burden and time-willing-to travel for vaccination, the early allocation scheme favored spatial accessibility within US metropolitan areas, in contrast to rural areas that were more likely to have both more vulnerable populations and more vaccine deserts. At the time of the analysis, the authors estimated that about 14% of the US population was living in vaccine deserts.

  Rader et al. (June 12, 2021). Spatial Accessibility Modeling of Vaccine Deserts as Barriers to Controlling SARS-CoV-2 Transmission. Pre-print downloaded Jun 14 from https://doi.org/10.1101/2021.06.09.21252858

- A modeling study estimating the impact of different non-pharmaceutical intervention (NPI) policies on the SARS-CoV-2 effective reproduction number (R_{eff}) found that NPIs that included closure of schools and leisure activities and nursing home visiting bans were all associated with a median R_{eff} below 1 when combined with either stay at home orders (median R_{eff} 0.97) or face masks (median R_{eff} 0.97). The authors note that the simultaneous implementation of multiple NPI policies makes it difficult to estimate the effect of any one policy, particularly school closures. Lifting restrictions on leisure activities (e.g., restaurants and gyms) was associated with increased R_{eff}, indicating higher transmission risks, while less dramatic changes in R_{eff} were estimated for the removal of stay-at-home orders and medical service suspension. The authors suggest that these results indicate that relaxation of some NPIs will need to be counterbalanced by continuation and/or implementation of others.

  Yang et al. (June 2021). Effect of Specific Non-Pharmaceutical Intervention Policies on SARS-CoV-2 Transmission in the Counties of the United States. Nature Communications. https://doi.org/10.1038/s41467-021-23865-8

Public Health Policy and Practice

- *[Pre-print, not peer-reviewed]* A cohort study of over 29 million adults in the UK found that compared to people without disabilities, mortality involving COVID-19 was higher both among people who self-identified as more-disabled (HR=3.1) and less-disabled (HR=1.9). Between January 24, 2020 and February 28, 2021, >100,000 people in the UK died from COVID-19-related causes, 58% of whom had disabilities. Among people aged 30-69, mortality involving COVID-19 risk was 8.5-fold higher among females who were more-disabled and 5.4-fold higher among more-disabled males.

  Bosworth et al. (June 13, 2021). Deaths Involving COVID-19 by Disability Status a Retrospective Analysis of 29 Million Adults during the First Two Waves of the Coronavirus Pandemic in England. Pre-print downloaded Jun 14 from https://doi.org/10.1101/2021.06.10.21258693

- An online cross-sectional survey conducted in May 2020 (n=963) found that experiencing structural discrimination was associated with higher health-specific COVID-19 conspiracy beliefs, while everyday discrimination was associated with more general medical mistrust but not with health-specific COVID-19 conspiracy beliefs. In addition, higher endorsement of health-specific COVID-19 conspiracy beliefs, but not general medical mistrust, was associated with significantly lower engagement in health-specific COVID-19 conspiracy beliefs.

Smith et al. (June 2021). An Investigation of Associations Between Race, Ethnicity, and Past Experiences of Discrimination with Medical Mistrust and COVID-19 Protective Strategies. Journal of Racial and Ethnic Health Disparities. https://doi.org/10.1007/s40615-021-01080-x

Other Resources and Commentaries

- Portal Vein Thrombosis Associated with ChAdOx1 NCov-19 Vaccination – The Lancet Gastroenterology & Hepatology (June)
- COVID-19 Vaccine: The Gender Disparity – Journal of Perinatal Medicine (June 11)
- High Food Insecurity in Latinx Families and Associated COVID-19 Infection in the Greater Bay Area, California – BMC Nutrition (June)
- Zoonotic and Reverse Zoonotic Transmissibility of SARS-CoV-2 – Virus Research (June)
- The Impact of Financialisation on Public Health in Times of COVID-19 and Beyond – Sociology of Health & Illness (June)
- Narrative Complexity in the Time of COVID-19 – The Lancet (June)
- DNA Test to Predict Odds of Severe COVID-19 Draws Scrutiny – Science (June 11)
- Does Vaccinating Adults Stop Kids from Spreading COVID Too – Nature (June 10)
- Topics and Sentiments in COVID-19 Vaccine-Related Discussion on Twitter – Journal of Medical Internet Research (June)
- Management of COVID-19 in a Deployed Setting – Military Medicine (June)
- Mitigating SARS-CoV-2 in the Deployed Environment – Military Medicine (June)
- Maternal and Neonatal SARS-CoV-2 Antibodies Assessment after MRNA Maternal Vaccination in the Third Trimester of Pregnancy – International Journal of Gynaecology and Obstetrics (June)
- Of Mice and Schoolchildren: A Conceptual History of Herd Immunity – American Journal of Public Health (June)
- Characterizing the Impact of COVID-19 on Pre-Exposure Prophylaxis (PrEP) Care – AIDS and Behavior (June)
- Implications of mRNA-Based SARS-CoV-2 Vaccination for Cancer Patients – Journal for Immunotherapy of Cancer (June)
- Implications of SARS-CoV-2 Viral Load in Children – JAMA Pediatrics (June 11)
- On the Usage of Combined Data Structures to Study COVID-19 in Understudied Populations – JAMA Network Open (June)
- Alcohol-Related Harm during the COVID-19 Pandemic – The Lancet Gastroenterology & Hepatology (July)
- The Incubation Period Distribution of Coronavirus Disease 2019 (COVID-19): A Systematic Review and Meta-Analysis – Clinical Infectious Diseases (June)

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