2019-nCoV Literature Situation Report (Lit Rep)

April 8, 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 single dose of the Pfizer-BioNTech vaccine substantially increased neutralizing activity against SARS-CoV-2 variants B.1.1.7, B.1.351, and P.1 among 6 previously infected healthcare workers. Geometric mean titers against B.1.351 increased by 228-fold.** More
- **The B.1.1.7 SARS-CoV-2 variant rapidly became the dominant circulating strain in the greater Toronto, Canada area between December 2020 and March 2021.** More
- **Only 37% of residents of nursing homes in Belgium who did not have a prior history of SARS-CoV-2 infection had vaccine-elicited humoral and cellular responses within 1 week of the second doses of the Pfizer-BioNTech vaccine, compared to 97% of residents with a history of prior infection and 87% of infection-naïve health care workers.** More
- **Nearly 1 in 5 individuals with comorbid conditions expressed COVID-19 vaccine hesitancy in an international cross-sectional survey (n=22,000, 74% from the US). Factors associated with hesitancy included younger age, female gender, belonging to an ethnic minority group, and distrust of media coverage.** More

Transmission

- *[Pre-print, not peer-reviewed] In vitro* experiments show that while the P681H mutation found in the SARS-CoV-2 B.1.1.7 variant was associated with more efficient cleavage of the Spike 1 and Spike 2 (S1/S2) subunits, this did not translate to a significant impact on cell entry or an increase in cell-to-cell spread.

  Lubinski et al. (Apr 8, 2021). Functional Evaluation of Proteolytic Activation for the SARS-CoV-2 Variant B.1.1.7 Role of the P681H Mutation. Pre-print downloaded Apr 8 from https://doi.org/10.1101/2021.04.06.438731

Geographic Spread

- The B.1.1.7 SARS-CoV-2 variant (first described in the UK) rapidly became the dominant circulating strain in the greater Toronto, Canada area between December 2020 and March 2021. Based on PCR S-gene target failure, which is strongly associated with the B.1.1.7 variant, 2% of samples were inferred to be the B.1.1.7 variant in mid-December 2020, which increased to 75% by March 31, 2021.

Brown et al. (Apr 8, 2021). S-Gene Target Failure as a Marker of Variant B.1.1.7 Among SARS-CoV-2 Isolates in the Greater Toronto Area, December 2020 to March 2021. JAMA. https://doi.org/10.1001/jama.2021.5607

Testing and Treatment

- US Veterans who are female, from racial/ethnic minority groups, had a low income, or had a service-related disability were more likely to obtain a COVID-19 test according to a retrospective cohort study with over 6 million veterans across 130 Veterans Health Administration facilities. Among veterans who were tested, those who identify as African American or native Hawaiian/Other Pacific Islander were 13% more likely to test positive than white veterans, while veterans who identify as Hispanic/Latino were 43% more likely to test positive than non-Hispanic/Latino veterans.

  Ferguson et al. (Apr 7, 2021). Differences in COVID-19 Testing and Test Positivity Among Veterans, United States, 2020. Public Health Reports. https://doi.org/10.1177/00333549211009498

- *[Pre-print, not peer-reviewed]* Treatments for SARS-CoV-2 infection designed to inhibit SARS-CoV-2 transmembrane serine protease 2 (TMPRSS2) and RNA-dependent RNA-polymerase (RdRp), proteins that play a role in cell entry, were shown to suppress *in vitro* viral replication of both variants of concern B.1.1.7 and B.1.351 with similar effectiveness as compared to the parent SARS-CoV-2 strain. Drug candidates tested included four TMPRS22 inhibitors (camostat, nafamostat, aprotinin, and bromhexine) and two RdRp inhibitors (remdesivir and molnupiravir). The authors note that the lack of substantial differences in drug efficacy among the three lineages suggests the potential targets of these drugs lie outside the mutations present in the two variants.

  Lee et al. (Apr 8, 2021). TMPRSS2 and RNA-Dependent RNA Polymerase Are Effective Targets of Therapeutic Intervention for Treatment of COVID-19 Caused by SARS-CoV-2 Variants (B.1.1.7 and B.1.351). Pre-print downloaded Apr 8 from https://doi.org/10.1101/2021.04.06.438540

- *[Pre-print, not peer-reviewed]* The monoclonal antibody (mAb) treatment CERC-002 reduced mortality and the risk of respiratory failure through day 28 compared to placebo (84% vs 65%; p=0.044) among hospitalized COVID-19 patients with mild-to-moderate acute respiratory distress syndrome (ARDS) according to a randomized placebo-controlled study (n=83). Efficacy was highest among patients ≥60 years old (77% vs 47%; p=0.042).

  Perlin et al. (Apr 7, 2021). CERC-002 a Human Anti-LIGHT mAb Reduces Respiratory Failure and Death in Hospitalized COVID-19 ARDS Patients. Pre-print downloaded Apr 8 from https://doi.org/10.1101/2021.04.03.21254748

Vaccines and Immunity

- A single dose of the Pfizer-BioNTech vaccine substantially increased neutralizing activity against SARS-CoV-2 variants B.1.1.7, B.1.351, and P.1 among healthcare workers (HCWs) previously infected with SARS-CoV-2 (n=6). Serum samples from each HCW were obtained 1-12 weeks after natural infection, immediately before vaccination, and 1-2 weeks after vaccination and were tested using a microneutralization assay containing isolates of the parent strain and SARS-CoV-2 variants. Geometric mean titers (GMTs) for neutralizing activity were low prior to vaccination against the parent strain, B.1.1.7, P.1, and B.1.351 variants (GMTs: 81, 40, 36, and 7, respectively), but increased

by 114-, 203-, 81-, and 228-fold after vaccination, respectively (corresponding GMTs: 9195, 8192, 2896, and 1625).

Lustig et al. (Apr 7, 2021). Neutralizing Response against Variants after SARS-CoV-2 Infection and One Dose of BNT162b2. New England Journal of Medicine. https://doi.org/10.1056/NEJMc2104036

- Antibody responses to the B.1.351 SARS-CoV-2 variant (aka, 501Y.V2) in a cohort of patients hospitalized with COVID-19 in South Africa (n=89) were found to be robust and showed high levels of cross-reactivity against the virus strain from the first wave. Furthermore, sera from patients infected with B.1.351 also neutralized the P.1 variant (aka, 501Y.V3) first described in Brazil, suggesting that the antibody response in patients infected with the B.1.351 variant has high levels of cross-reactivity across variants. The authors suggest that these results indicate that vaccines built on the spike protein of B.1.351 may be promising candidates for elicitating cross-reactive neutralizing antibody responses to SARS-CoV-2. *[EDITORIAL NOTE: A pre-print version of this article was summarized in this report on March 10, 2021].*

  Moyo-Gwete et al. (Apr 7, 2021). Cross-Reactive Neutralizing Antibody Responses Elicited by SARS-CoV-2 501Y.V2 (B.1.351). New England Journal of Medicine. https://doi.org/10.1056/NEJMc2104192

- *[Pre-print, not peer-reviewed]* Phase 1b trials for a novel adenovirus-vector COVID-19 vaccine (hAd5-S-Fusion+N-ETSD developed by ImmunityBio) containing the SARS-CoV-2 antigen spike (S) and nucleocapsid (N) proteins demonstrated a 10-fold increase in mean S- and N-specific T-cell responses from patients (n=4) with prior SARS-CoV-2 infection after a single dose. For context, currently approved vaccines only target the S protein. Modeling predictions suggest that the elicited T-cell responses could be robust against the parent SARS-CoV-2 strain and variants of concern.

  Sieling et al. (Apr 7, 2021). Single Prime HAd5 Spike (S) + Nucleocapsid (N) Dual Antigen Vaccination of Healthy Volunteers Induces a Ten-Fold Increase in Mean S- and N- T-Cell Responses Equivalent to T-Cell Responses from Patients Previously Infected with SARS-CoV-2. Pre-print downloaded Apr 8 from https://www.medrxiv.org/content/10.1101/2021.04.05.21254940v1

- *[Pre-print, not peer-reviewed]* Nearly 1 in 5 individuals with serious comorbid conditions expressed COVID-19 vaccine hesitancy in an international cross-sectional survey conducted from January to February 2021. Participants (n=22,000, 74% from the US) were randomly sampled from Inspire, a large online health community of individuals with comorbid conditions. 10% of participants declared they would not get vaccinated, 4% stated they probably would not, and 5% were not sure they would agree to vaccination (total hesitancy 19%). Factors associated with hesitancy included younger age, female gender, belonging to an ethnic minority group, and distrust of media coverage. 25% of participants reported receiving at least one dose of a COVID-19 vaccine, 29% of whom were US participants.

  Tsai et al. (Apr 7, 2021). COVID-19 Vaccine Hesitancy among Individuals with Cancer Autoimmune Diseases and Other Serious Comorbid Conditions. Pre-print downloaded Apr 8 from https://doi.org/10.1101/2021.04.06.21254014

- Nursing home residents who had a prior SARS-CoV-2 infection were more likely than those with no history of infection to have an immunologic response within 1 week of the second dose of the Pfizer-BioNtech vaccine. Among nursing home residents in Belgium, humoral and cellular responses elicited by vaccination with the Pfizer-BioNtech vaccine were detected in 97% of those with prior SARS-CoV-2 infection (n=64) 1 week after the second dose (4 weeks after the first dose) but in only 37% of infection-naïve residents (n=46). In comparison, vaccine-elicited humoral and cellular responses were detected in 87% of 15 infection-naïve healthcare workers serving as controls.

  Van Praet et al. (Apr 7, 2021). Humoral and Cellular Immunogenicity of the BNT162b2 MRNA Covid-19 Vaccine in Nursing Home Residents. Clinical Infectious Diseases. https://doi.org/10.1093/cid/ciab300

Clinical Characteristics and Health Care Setting

- Anti-hypertensive medications, including angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), and calcium channel blockers (CCB), were not associated with mortality among hospitalized COVID-19 patients in a retrospective cohort study (n=841). However, use of ACEI/ARB and ACEI/ARB combined with CCB were associated with a 42% and 45% lower risk of ICU admission, respectively. Among patients with a history of hypertension (n=453), ACEI use was associated with a 71% lower risk of in-house mortality.

  Choksi et al. (Apr 7, 2021). Outcomes of Hospitalized COVID-19 Patients Receiving Renin Angiotensin System Blockers and Calcium Channel Blockers. American Journal of Nephrology. https://doi.org/10.1159/000515232

Mental Health and Personal Impact

- African American and Hispanic individuals, women, and households with low income were disproportionately affected by adverse social and mental health outcomes during lockdown in the first wave of the COVID-19 pandemic according to a large population-representative cross-sectional survey of over 1 million US respondents from April to July 2020. On average, every 10% reduction in mobility was associated with higher odds of unemployment, mental health problems, and class cancellations. Compared to high-income white men, low-income African American men experienced the highest risks of food insufficiency (OR=3.3), unemployment (OR=2.8), and rent/mortgage defaults (OR=5.7), while women had a 2-fold elevated risk of mental health problems and medical care inaccessibility. Disproportionately affected high risk groups also included Hispanic men with a low income and women with a low income across all races/ethnicities.

  Chakrabarti et al. (Apr 7, 2021). Association of Human Mobility Restrictions and Race/Ethnicity–Based, Sex-Based, and Income-Based Factors With Inequities in Well-Being During the COVID-19 Pandemic in the United States. JAMA Network Open. https://doi.org/10.1001/jamanetworkopen.2021.7373

- 44% (32 of 73) of African American patients who were admitted to the ICU and underwent invasive mechanical ventilation for COVID-19 were diagnosed with major depressive disorder (MMD) within 90 days of discharge. Patients were identified during depression screening following discharge from a hospital in Atlanta, Georgia. MDD was more frequently diagnosed in women than men (69% vs 29%), and in patients aged >75 years (66%) and those with multiple comorbidities (45%). Of the 37%

(27 of 73) diagnosed with moderately severe to severe depression, only 26% were receiving treatment for depression at the time of screening.

Olanipekun et al. (Apr 6, 2021). Incidence and Severity of Depression Among Recovered African Americans with COVID-19-Associated Respiratory Failure. Journal of Racial and Ethnic Health Disparities. https://doi.org/10.1007/s40615-021-01034-3

Other Resources and Commentaries

- The Mobility Gap: Estimating Mobility Thresholds Required to Control SARS-CoV-2 in Canada – Canadian Medical Association Journal (Apr 7)
- Digital Herd Immunity and COVID-19 – Physical Biology (Apr 7)
- No-Jab, No-Job Clause: Ethical Issues and Legal Impediments – Journal of Public Health (Apr 7)
- An Informative Discussion for School Nurses on COVID-19 MRNA Vaccine – NASN School Nurse (Apr 7)
- Symptoms and Functional Impairment Assessed 8 Months After Mild COVID-19 Among Health Care Workers – JAMA (Apr 7)
- Prognostic Model to Identify and Quantify Risk Factors for Mortality among Hospitalised Patients with COVID-19 in the USA – BMJ Open (Apr 7)
- Experiences, Impacts and Mental Health Functioning during a COVID-19 Outbreak and Lockdown: Data from a Diverse New York City Sample of College Students – PLOS ONE (Apr 7)
- Comparable Environmental Stability and Disinfection Profiles of the Currently Circulating SARS-CoV-2 Variants of Concern B.1.1.7 and B.1.351 – BioRxiv (Apr 8)
- The Impact of COVID-19 on American Indian and Alaska Native Communities: A Call for Better Relational Models – American Journal of Public Health (May 1)
- Contact Tracing Could Exacerbate COVID-19 Health Disparities: The Role of Economic Precarity and Stigma – American Journal of Public Health (May 1)
- Polyethylene Glycol (PEG) Is a Cause of Anaphylaxis to the Pfizer/BioNTech MRNA COVID-19 Vaccine – Clinical & Experimental Allergy (Apr 6)
- Neutralization of SARS-CoV-2 Variants B.1.429 and B.1.351 – The New England Journal of Medicine (Apr)
- Correction: Association between Influenza Vaccination and Hospitalisation or All-Cause Mortality in People with COVID-19: A Retrospective Cohort Study – BMJ Open Respiratory Research (Apr 7)
- Responding to Pandemics and Other Disease Outbreaks in Homeless Populations: A Review of the Literature and Content Analysis – Health & Social Care in the Community (Apr 6).

Report prepared by the UW Alliance for Pandemic Preparedness and Global Health Security and the START Center in collaboration with and on behalf of WA DOH COVID-19 Incident Management Team