2019-nCoV Literature Situation Report (Lit Rep)

March 5, 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

- **Mask mandates in the US were associated with decreases in the growth rate of daily COVID-19 cases and deaths after implementation during March-December 2020. During the same period, reopening of any on-premises dining was associated with increases in the growth rates of daily COVID-19 cases and deaths.** More
- **Use of the antibiotic azithromycin plus usual care did not provide meaningful benefits to recovery time from COVID-19 compared to usual care alone, based on findings from a randomized, placebo-controlled, open-label trial in the UK.** More
- **In two separate randomized trials, the anti-IL-6 receptor monoclonal antibody treatments tocilizumab and sarilumab did not improve outcomes in patients hospitalized with COVID-19.** More and More

Non-Pharmaceutical Interventions

- A comparison of US county-level data on mask mandates and restaurant re-openings in relation to county-level changes in COVID-19 case and death growth rates across the country (n=3,142 counties) between March-December 2020 found mask mandates were associated with decreases in daily COVID-19 case and death growth rates in all intervals from 1-20 to 81-100 days after implementation, as well as reduced SARS-CoV-2 transmission.
- Allowing any on-premises dining was associated with increases in daily COVID-19 case growth rates by 41-60 after reopening and through 81-100 days after reopening. Restaurant reopening was also associated with increases in the death growth rate within 61-80 days and through 80-100 days.
- Associations between policies and COVID-19 outcomes were measured using a reference period (1-20 days before implementation), and growth rates were defined as percentage point change. Regression models controlled for several covariates, including bar closures, stay at home orders, bans on gatherings of ≥10 persons, daily SARS-CoV-2 tests 100,000 persons, county and time.

  Guy et al. (Mar 5, 2021). Association of State-Issued Mask Mandates and Allowing On-Premises Restaurant Dining with County-Level COVID-19 Case and Death Growth Rates — United States, March 1–December 31, 2020. MMWR. https://doi.org/10.15585/mmwr.mm7010e3

Transmission

- *[Pre-print, not peer-reviewed]* An analysis of saliva specimens collected through a campus-wide surveillance program for SARS-CoV-2 among students at the University of Colorado, Boulder during the Fall academic semester of 2020 found that 2% (1,405 of 72,500 specimens tested) of the

samples were positive for SARS-CoV-2. All of the positive students self-reported no symptoms on the day of collection. Residents of dormitories were tested weekly (August 27–December 11, 2020), and several campus testing sites offered testing for any campus affiliate. Viral load levels in the asymptomatic students had similar distributions compared to hospitalized symptomatic individuals from reference studies.

Yang et al. (Mar 5, 2021). Just 2% of SARS-CoV-2-Positive Individuals Carry 90% of the Virus Circulating in Communities. Pre-print downloaded Mar 5 from https://doi.org/10.1101/2021.03.01.21252250

Testing and Treatment

- Use of the antibiotic azithromycin plus usual care did not provide meaningful benefits to recovery time from COVID-19 compared to usual care alone, according to a randomized, placebo-controlled, open-label trial in the UK from May to November 2020. Patients receiving azithromycin plus usual care (n=500) had similar time to recovery compared to patients receiving usual care alone (n=823) (HR=1.08, 95%CI: 0.95-1.23). The probability of a clinically meaningful benefit of at least 1.5 days in time to recovery was 0.23. Both groups had similar rates of hospitalization (3%).

  Butler et al. (Mar 4, 2021). Articles Azithromycin for Community Treatment of Suspected COVID-19 in People at Increased Risk of an Adverse Clinical Course in the UK (PRINCIPLE): A Randomised, Controlled, Open-Label, Adaptive Platform Trial. The Lancet. https://doi.org/10.1016/S0140-6736(21)00461-X

- A multi-center, phase-3, randomized trial among patients (n=180) with moderate to severe COVID-19 conducted at 12 hospitals across India of the anti-IL-6 receptor monoclonal antibody treatment tocilizumab found no significant difference in the proportion of patients with progressive COVID-19 up to day 14 between the treatment group compared to standard care group (9% vs 13%). No significant difference between the two groups was observed in the secondary endpoints, as well as the proportion of patients experiencing adverse events, serious adverse events, or death.

  Soin et al. (Mar 4, 2021). Tocilizumab plus Standard Care versus Standard Care in Patients in India with Moderate to Severe COVID-19-Associated Cytokine Release Syndrome (COVINTOC): An Open-Label, Multicentre, Randomised, Controlled, Phase 3 Trial. The Lancet Respiratory Medicine. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00081-3/fulltext

- In a randomized, placebo-controlled, double-blind trial, the IL-6 receptor inhibitor sarilumab did not reduce the median time to improvement by day 29 among patients hospitalized for COVID-19 compared to placebo (n=416). Patients receiving placebo had a median time to improvement of 12 days, compared to 10 days among those receiving either 200 mg or 400 mg of sarilumab (HR=1.03 and HR=1.14, respectively). No significant differences were observed in proportions of patients alive by day 29 across the three groups.

  Lescure et al. (Mar 4, 2021). Sarilumab in Patients Admitted to Hospital with Severe or Critical COVID-19: A Randomised, Double-Blind, Placebo-Controlled, Phase 3 Trial. The Lancet Respiratory Medicine. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00099-0/fulltext

Vaccines and Immunity

- Most convalescent sera from people who had recovered from mild COVID-19 (n=29) and virtually all Pfizer-BioNTech mRNA vaccine-induced immune sera (n=24) were shown to have diminished

neutralizing activity against engineered SARS-CoV-2 strains including a chimeric strain combining a strain identified in Washington state with a B.1.351 spike gene (Wash SA-B.1.351 strain), or recombinant viruses containing mutations at position 484 and 501. Several highly neutralizing monoclonal antibodies (mAbs) lost inhibitory activity against Wash SA-B.1.351 or recombinant variants with an E484K spike mutation. The authors note that targeting of highly conserved regions, enhancement of mAb potency, or adjustments to the spike sequences of vaccines may be needed to prevent loss of protection *in vivo*. *[EDITORIAL NOTE: A Pre-print related to this manuscript was summarized on January 17, 2021]*

Chen et al. (Mar 4, 2021). Resistance of SARS-CoV-2 Variants to Neutralization by Monoclonal and Serum-Derived Polyclonal Antibodies. Nature Medicine. https://doi.org/10.1038/s41591-021-01294-w

- A prospective serology cohort study among UK healthcare workers found that by 21 weeks, 22% (31 of 143) of those previously positive for anti-SARS-CoV-2 spike (S1) antibodies reverted to being S1 negative, while only 4% (6 of 150) of those previously positive for anti-SARS-CoV-2 nucleocapsid (NP) antibodies reverted to being NP negative, which the authors suggest may indicate that anti-S mediated humoral immunity in some individuals may not persist long after the initial post-infection period. Additionally, while both anti-S1 and anti-NP measurements correlated well, only anti-S1 measurements correlated with neutralizing antibody titers. Mathematical modelling showed that anti-S1 antibodies cleared faster compared to anti-NP antibodies (median half-life 2.5 weeks vs 4 weeks), transitioned earlier to decreased antibody production (median 8 vs 13 weeks), and had lower relative production rates after the transition (median 35% vs 50%).

  Manisty et al. (Mar 2, 2021). Time Series Analysis and Mechanistic Modelling of Heterogeneity and Sero-Reversion in Antibody Responses to Mild SARS-CoV-2 Infection. EBioMedicine. https://doi.org/10.1016/j.ebiom.2021.103259

- *[Pre-print, not peer-reviewed]* Among 176 participants receiving two doses of the Pfizer-BioNTech vaccine in a cohort study in Germany, participants aged >80 years had lower SARS-CoV-2 specific IgG antibody titers and neutralizing titers compared to participants aged <60 years after each dose. While the IgG titer increase between the first and second dose was larger among older participants, mean IgG titers 17 days after the second dose were much lower compared to younger participants. The neutralizing antibody response was similarly lower in older recipients, with only 69% of older participants having detectable neutralizing antibody titers 17 days after the second dose, compared to 98% of younger participants.

  Müller et al. (Mar 5, 2021). Age-Dependent Immune Response to the BioNtech-Pfizer BNT162b2 COVID-19 Vaccination. Pre-print downloaded Mar 5 from https://doi.org/10.1101/2021.03.03.21251066

- *[Pre-print, not peer-reviewed]* An *in vitro* study of newly-emerging SARS-CoV-2 mutations in the receptor binding domain (RBD) of the viral spike protein found in the P.1 variant (first described in Brazil) demonstrated increased angiotensin-converting enzyme 2 (ACE2) affinity for the mutant RBD and reduced neutralization ability of immune sera induced from prior strains. RBD mutations at K417N, E484K and N501Y resulted in increased affinity of SARS-CoV-2 for ACE2 by a factor of 2. Both mouse immune-induced sera and human sera from convalescent patients showed reduced capacity to block binding of ACE2 in mutant RBD, providing evidence that the P.1 variant may be more infectious and less susceptible to neutralization by antibodies induced with previous strains.

Vogel et al. (Mar 4, 2021). SARS-CoV-2 Variant with Higher Affinity to ACE2 Shows Reduced Sera Neutralization Susceptibility. Pre-print downloaded Mar 5 from https://doi.org/10.1101/2021.03.04.433887

- A retrospective cohort study using routinely collected health records from patients with COVID-19 (n= 6,921) in South West England between January and July 2020 found that receiving the influenza vaccination sometime between January 1, 2019 and COVID-19 diagnosis was associated with a 15% reduced odds of all-cause mortality or hospitalization (aOR=0.85), and a 24% reduced odds of all-cause mortality alone. Differences between vaccinated and unvaccinated individuals was accounted for using a propensity score.

  Wilcox et al. (Mar 4, 2021). Association between Influenza Vaccination and Hospitalisation or All-Cause Mortality in People with COVID-19: A Retrospective Cohort Study. BMJ Open Respiratory Research. https://doi.org/10.1136/bmjresp-2020-000857

Clinical Characteristics and Health Care Setting

- Asthma was associated with a higher likelihood over developing more severe COVID-19. Among more than 75,000 patients hospitalized with COVID-19 in the UK from January to August 2020, patients with asthma were 1.2-times as likely to receive critical care compared to patients without underlying respiratory conditions, regardless of comorbidities and disease severity at admission. Patients aged 16 years and older with severe asthma had a significantly higher risk of mortality than those with no asthma (aOR=1.2). Patients aged 50 and older with chronic pulmonary disease were less likely than those without a respiratory condition to receive critical care regardless of asthma status, but had a 1.2-fold higher mortality risk regardless of inhaled corticosteroid use. However, use of inhaled corticosteroids within 2 weeks of admission was associated with a 14% reduction in mortality risk.

  Bloom et al. (Mar 4, 2021). Articles Risk of Adverse Outcomes in Patients with Underlying Respiratory Conditions Admitted to Hospital with COVID-19: A National, Multicentre Prospective Cohort Study Using the ISARIC WHO Clinical Characterisation Protocol UK. The Lancet Respiratory Medicine. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00013-8/fulltext

Public Health Policy and Practice

- A qualitative study of tobacco use and purchasing behaviors in the US between April and May 2020 during the COVID-19 lockdown found that most participants (n=44) increased use, which was predominantly driven by individual-level factors such as pandemic-related anxiety, boredom, and irregular routines. Individuals who reported decreased use cited social drivers, such as fewer interpersonal interactions and fear of sharing products as reasons for their change in use. Users of electronic nicotine delivery systems, also known as e-cigarettes or vapes, reported being driven to purchase products online due to decreased accessibility within the community.

  Giovenco et al. (Mar 1, 2021). Multi-Level Drivers of Tobacco Use and Purchasing Behaviors during COVID-19 "Lockdown": A Qualitative Study in the United States. The International Journal on Drug Policy. https://doi.org/10.1016/j.drugpo.2021.103175

Other Resources and Commentaries

- United States Response to the COVID-19 Pandemic, January-November 2020 – Health Economics, Policy and Law (Mar 5)

- SARS-CoV-2 on Ocular Surfaces in a Cohort of Patients With COVID-19 From the Lombardy Region, Italy – JAMA Ophthalmology (Mar 4)
- New Insights on COVID-19 and the Heart – JACC: Cardiovascular Imaging (Mar 1)
- COVID-19 in 2021—Continuing Uncertainty – JAMA (Mar 4)
- COVID-19 Guidelines for Pregnant Women and New Mothers: A Systematic Evidence Review – International Journal of Gynecology & Obstetrics (Mar 4)
- Assessment of Available Online Information About Nasopharyngeal Swab Testing in Patient Instructions for Sinus and Pituitary Surgery – JAMA Otolaryngology–Head & Neck Surgery (Mar 4)
- SARS-CoV-2 Variants and Ending the COVID-19 Pandemic – The Lancet (Feb 6)
- Early Assessment of Diffusion and Possible Expansion of SARS-CoV-2 Lineage 20I/501Y.V1 (B.1.1.7, Variant of Concern 202012/01) in France, January to March 2021 – Euro Surveillance: European Communicable Disease Bulletin (Mar 4)
- Avoiding Exploitation in Multinational Covid-19 Vaccine Trials – BMJ (Mar 4)
- Approaches for Optimal Use of Different COVID-19 Vaccines – JAMA (Mar 4)
- Comment IL-6 Blockade for COVID-19: A Global Scientific Call to Arms – The Lancet Respiratory Medicine (Mar 4)
- Comment Global Health Security Requires Endemic Disease Eradication – The Lancet (2021)
- COVID-19 Re-Infection: Diagnostic Challenges and Proposed Diagnostic Criteria – Diabetes & Metabolic Syndrome: Clinical Research & Reviews (Feb 11)
- Covid-19: 237m Vaccine Doses to Be Distributed Worldwide over next Three Months – BMJ (Mar 4)
- US Health Agency Will Invest $1 Billion to Investigate 'Long COVID. – Nature (Mar 4)
- Assessment of the Temporal Trajectory of Clinical Trials for COVID-19 Interventions After Highly Publicized Lay and Medical Attention – JAMA Network Open (Mar 4)

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