2019-nCoV Literature Situation Report (Lit Rep)

April 13, 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

- **Prior SARS-CoV-2 infection was associated with an 84% lower risk of infection according to the SIREN Study, a large cohort study of over 25,000 individuals. From June to December 2020, reinfections/infections were detected in 0.02% (155 of 8,278) of participants positive at baseline compared to 0.1% (1,704 of 17,383) of participants negative at baseline. The authors found no evidence that the emergence of the B.1.1.7 variant was linked to increased reinfection rates.** More
- **Infections with the B.1.1.7 variant of SARS-CoV-2 likely cause similar symptoms compared to pre-existing strains, according to an analysis of data from the COVID-19 Symptom Study obtained during a period when the B.1.1.7 variant was surging in the UK (September to December 2020). Types of symptoms, duration of symptoms, and reinfection rate were comparable to data obtained during outbreaks with pre-existing strains.** More
- **Vaccine-induced IgG antibodies were present in 97% of breastmilk samples from breastfeeding women 6 weeks after receiving the first dose of the Pfizer-BioNTech vaccine in a cohort study in Israel. No mothers or infants experienced any serious adverse events during the study period.** More
- **In a randomized, open-label trial of outpatients with COVID-19, the inhaled glucocorticoid budesonide reduced the rates of seeking medical attention or hospitalization when initiated within seven days of symptom onset.** More**. In a separate open label trial involving older adult outpatients within fourteen days of symptom onset, budesonide reduced the time to recovery by 3 days.** More

Transmission

- B.1.1.7 infections likely cause similar symptoms compared to pre-existing variants, according to an analysis of data from the COVID-19 Symptom Study app users obtained during a period when the B.1.1.7 variant was surging in the UK (September to December 2020). Participants reported no change in symptoms or disease duration. Only 0.7% of reports indicated possible reinfection (two positive tests separated by more than 90 days), suggesting that B.1.1.7 reinfections occurred with similar frequency compared to pre-existing variants. Reinfection occurrence also had stronger correlation with an overall regional rise in cases than with a regional increase in the proportion of B.1.1.7 infections as estimated by proportion of tests with Spike-Gene Target Failure. The authors also estimate that although Rt associated with B.1.1.7 was 1.4-times higher than pre-existing variants, B.1.1.7 Rt was reduced below 1 by lockdown measures even in regions with high proportions of B.1.1.7 infections.

Graham et al. (Apr 12, 2021). Changes in Symptomatology, Reinfection, and Transmissibility Associated with the SARS-CoV-2 Variant B.1.1.7: An Ecological Study. The Lancet Public Health. https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(21)00055-4/fulltext

- SARS-CoV-2 seroprevalence among children aged 1-10 years in Bavaria, Germany increased from 0.68% during the first wave (January-August 2020) to 3.92% during the second wave (September-February 2021). The authors suggest that the increase in seropositivity was likely caused by generally higher virus exposure during fall and winter, school openings, and the introduction of variants. By February 2021, genomic sequencing estimated that variants, particularly B.1.1.7, comprised up to 65% of infections in pre-school children and 70% in school-age children.

  Hippich et al. (Apr 3, 2021). A Public Health Antibody Screening Indicates a Marked Increase of SARS-CoV-2 Exposure Rate in Children during the Second Wave. Med. https://doi.org/10.1016/j.medj.2021.03.019

Testing and Treatment

- Treatment with the inhaled corticosteroid budesonide within 7 days of onset of mild COVID-19 symptoms was associated with a 91% reduction in risk of an urgent care visit, an emergency department consultation, or hospitalization. In the per-protocol analysis of the randomized, open-label phase 2 trial, one of these three outcomes occurred in 14% (10 of 70) of the usual care group compared to 1% (1 of 69) of the budesonide group. Clinical recovery was one day shorter in the budesonide group (7 vs 8 days) and fewer participants in the budesonide group had persistent symptoms at days 14 and 28. The trial was halted due to prioritization rules for clinical trials in the UK and was unable to meet the original sample size of 398 patients.

  Ramakrishnan et al. (Apr 9, 2021). Inhaled Budesonide in the Treatment of Early COVID-19 (STOIC): A Phase 2, Open-Label, Randomised Controlled Trial. The Lancet Respiratory Medicine. https://doi.org/10.1016/S2213-2600(21)00160-0

- *[Pre-print, not peer-reviewed]* The inhaled corticosteroid budesonide reduced time to recovery among older ambulatory SARS-CoV-2-infected adults by 3 days, according to an interim analysis of a randomized, open-label trial (PRINCIPLE Trial). In participants either 65 years and older without co-morbidities or less than 50 years with co-morbidities given 14 days of 800 mcg of budesonide twice daily, there were 59 out of 692 (8.5%) COVID-19 related hospitalizations/deaths in the budesonide group vs 100 out of 968 (10.3%) in the usual care group, a result which was not statistically significant (estimated percentage benefit, 2.1% [95% BCI −0.7% – 4.8%], probability of superiority 0.928). The authors note that not all participants had completed 28-day follow-up and that the study will have higher power to detect prevention of hospitalization once all data are analyzed.

  Yu et al. (Apr 12, 2021). Inhaled Budesonide for COVID-19 in People at Higher Risk of Adverse Outcomes in the Community Interim Analyses from the PRINCIPLE Trial. Pre-print downloaded Apr 13 from https://doi.org/10.1101/2021.04.10.21254672

Vaccines and Immunity

- Prior SARS-CoV-2 infection was associated with an 84% lower risk of new infection according to the SIREN Study, a large multi-center prospective study conducted in the UK from June to December 2020. During the study period, 155 potential reinfections were detected among 8,278 participants positive at baseline compared to 1,704 new PCR positive infections detected among 17,383 participants negative at baseline. This corresponds to 7.6 infections per 100,000 person-days in the

positive cohort, compared to 57.3 infections per 100,00 person-days in the negative cohort. Participants attended regular PCR (every 2 weeks) and antibody (every 4 weeks) testing and completed symptom and exposure questionnaires every 2 weeks. Although the B.1.1.7 variant was circulating during the final part of the study period, causing roughly 50% of infections, the authors did not find evidence that reinfection rates increased with increasing prevalence of B.1.1.7 infections.

Hall et al. (Apr 9, 2021). SARS-CoV-2 Infection Rates of Antibody-Positive Compared with Antibody-Negative Health-Care Workers in England: A Large, Multicentre, Prospective Cohort Study (SIREN). The Lancet. https://doi.org/10.1016/S0140-6736(21)00675-9

- SARS-CoV-2-specific IgG antibody levels were relatively stable for up to 6 months, whereas neutralizing antibody responses waned during that time, according to a cohort study of 34 adults with mild COVID-19. By 6 months, only 70% (23 of 33) of participants exhibited a neutralizing response compared to 91% or higher for IgG antibody responses. Presence of fever was associated with higher IgG antibody responses, while declining IgM antibody levels were strongly associated with declines in neutralizing activity.

  Harrington et al. (Mar 24, 2021). Rapid Decline of Neutralizing Antibodies Is Associated with Decay of IgM in Adults Recovered from Mild COVID-19 Disease. Cell Reports Medicine. https://doi.org/10.1016/j.xcrm.2021.100253

- More than half of people who died of COVID-19 in Ontario, Canada (3,475 of 6,728) had no record of hospitalization for treatment related to COVID-19 (up to February 2021). Hospitalizations were relatively uniform between ages 60-90 years, while deaths were more concentrated in ages 80 and above. Using a generalized linear model, the estimated probability of hospitalization given known infection was greatest among 80-81 year-olds at 28% and was below 5% among those aged <50 years. Estimated survival given hospitalization was estimated to be nearly 100% for those aged <40 years but declined with age down to 40% for those aged >100 years.

  Papst et al. (Dec 12, 2021). Age-Dependence of Healthcare Interventions for COVID-19 in Ontario, Canada. BMC Public Health. https://doi.org/10.1186/s12889-021-10611-4

- Vaccine-induced SARS-CoV-2-specific antibodies were found in a high proportion of breastmilk samples obtained up to 6 weeks post-vaccination from breastfeeding women in a cohort study in Israel (n=84,504 total samples). IgA antibody positivity peaked at 86% of samples at week 4 (1 week after second dose) and remained at 66% by week 6. IgG antibody levels remained low for the first 3 weeks but increased after week 4, with 97% of samples testing positive by weeks 5 and 6. No mother or infant experienced any serious adverse event during the study period. Consistent with other studies, more women reported a vaccine-related adverse event following the second dose compared to the first (62% vs 56%).

  Perl et al. (Apr 12, 2021). SARS-CoV-2–Specific Antibodies in Breast Milk After COVID-19 Vaccination of Breastfeeding Women. JAMA. https://doi.org/10.1001/jama.2021.5782

- 40% of nurses in Palestine reported planning to get a COVID-19 vaccine, according to a cross-sectional survey (n=639) conducted in January 2021. 41% would take it later when further protection and safety data were presented, and 18% would never take it. Preference for "natural immunity" and lack of vaccine knowledge were most strongly associated with vaccine hesitancy.

  Rabi et al. (Apr 12, 2021). Factors Affecting Nurses' Intention to Accept the COVID-9 Vaccine: A Cross-sectional Study. Public Health Nursing. https://doi.org/10.1111/phn.12907

Clinical Characteristics and Health Care Setting

- 26% of patients admitted for COVID-19 (n=963) to the Johns Hopkins Health System between March and May of 2020 had either a possible, probable, or confirmed hospital acquired infection (HAI). Independent risk factors for development of probable/confirmed HAI included history of congestive heart failure, dexamethasone during hospitalization, ICU admission prior to HAI, and receipt of antibiotics within 2 days of hospitalization. Of the 5% (62 of 963) patients confirmed HAI, bacteremia and bacterial pneumonia were the most common.

  Smith et al. (Apr 13, 2021). Hospital-Acquired Infections among Adult Patients Admitted for COVID-19. Infection Control & Hospital Epidemiology. https://doi.org/10.1017/ice.2021.148

Other Resources and Commentaries

- A Randomized, Double-Blind, Placebo-Controlled Phase 1 Trial of Inhaled and Intranasal Niclosamide: A Broad Spectrum Antiviral Candidate for Treatment of COVID-19 – The Lancet Regional Health - Europe (Apr 6)
- Mobilizing a COVID-19 Contact Tracing Workforce at Warp Speed: A Framework for Successful Program Implementation – The American Journal of Tropical Medicine and Hygiene (Apr 12)
- Genomic characteristics and clinical effect of the emergent SARS-CoV-2 B.1.1.7 lineage in London, UK: a whole-genome sequencing and hospital-based cohort study – The Lancet Infectious Diseases (Apr 13)
- Impact of COVID -19 Pandemic on the Mental Health of Students From 2 Semi-Rural High Schools in Georgia* – Journal of School Health (April 12)
- Predictors of Willingness to Get a COVID-19 Vaccine in the U.S – BMC Infectious Diseases (Apr 12)
- Buprenorphine Opioid Treatment During the COVID-19 Pandemic – JAMA Internal Medicine (Apr 12)
- Age-Based Healthcare Stereotype Threat during the COVID-19 Pandemic – Journal of Gerontological Social Work (Apr 12)
- Inadequate Reporting of COVID-19 Clinical Studies: A Renewed Rationale for the Sex and Gender Equity in Research (SAGER) Guidelines – BMJ Global Health (Apr 12)
- A Practical Approach to Filtering Facepiece Respirator Decontamination and Reuse: Ultraviolet Germicidal Irradiation – Current Treatment Options in Infectious Diseases (Apr 6)
- Caring for Individuals With Intellectual and Developmental Disabilities in the COVID-19 Crisis – Neurology: Clinical Practice (May 29, 202AD)
- A Systematic Review of Health Sector Responses to the Coincidence of Disasters and COVID-19 – BMC Public Health (Apr 13)
- Non-Invasive Adapted N-95 Mask Sampling Captures Variation in Viral Particles Expelled by COVID-19 Patients: Implications in Understanding SARS-CoV2 Transmission – PLOS ONE (Apr 12)
- Stress and Coping among Pregnant Black Women during the COVID-19 Pandemic – Public Health Nursing (Boston, Mass.) (Apr 12)

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