2019-nCoV Literature Situation Report (Lit Rep)

November 16, 2020

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

➢ **The incidence of out-of-hospital cardiac arrest was higher, while survival was lower, during the first weeks of the COVID-19 pandemic in the US, compared to one year prior. More**

➢ **A modeling study found that a SARS-CoV-2 vaccine with prophylactic efficacy of 70% could eliminate infection and prevent major outbreaks in a scenario where 80% of the population is vaccinated. More**

➢ **Moderna's mRNA-1273 COVID-19 vaccine demonstrated 94.5% efficacy in an interim analysis of data from the Phase 3 COVE study. More**

➢ **Patients hospitalized with COVID-19 who were treated with inhaled nebulized interferon beta-1a (SNG001) had greater odds of improvement and recovered more rapidly than those who received placebo. More**

Transmission

• Results from a SARS-CoV-2 PCR-based screening campaign found a high proportion of asymptomatic infection among residents and staff of long-term care facilities in France, with higher frequencies among residents than staff (13.4% versus 8.7%). Among infected residents, 16.4% were detected based on symptoms and 83.6% through mass screening. While many SARS-CoV-2 positive residents had respiratory symptoms (44.5%) and fever (46.5%), 23.0% were asymptomatic. Mortality was positively associated with male sex (OR = 3.95), age > 85 years (OR = 2.43) and receiving oxygen therapy (OR = 5.16) and was negatively associated with detection through mass screening (OR = 0.20) and receiving hydroxychloroquine and azithromycin treatment for more than 3 days (OR = 0.37).

  Ly et al. (Nov 2020). Pattern of SARS-CoV-2 Infection among Dependant Elderly Residents Living in Long-Term Care Facilities in Marseille, France, March–June 2020. International Journal of Antimicrobial Agents. https://doi.org/10.1016/j.ijantimicag.2020.106219

Testing and Treatment

• A phase 2 randomized, double-blind, placebo-controlled trial of inhaled nebulized interferon beta-1a (SNG001) for patients hospitalized with COVID-19 (n=101) found that patients who received the study drug had greater odds of improvement on the WHO ordinal scale for clinical improvement (OSCI) (OR = 2.32) on day 15 or 16 and were more likely to recover to an OSCI score of 1 (no limitation of activities) during treatment (HR = 2.19) compared to placebo. 66 (67%) patients required supplemental oxygen at enrollment (29 in the placebo group and 37 in the study drug

group). Headaches were the most frequently reported adverse event (15% vs. 10% in the study drug and placebo groups, respectively). Three deaths occurred in the placebo group and none in the study drug group.

> *Monk et al. (Nov 2020). Safety and Efficacy of Inhaled Nebulised Interferon Beta-1a (SNG001) for Treatment of SARS-CoV-2 Infection: A Randomised, Double-Blind, Placebo-Controlled, Phase 2 Trial. The Lancet Respiratory Medicine.* https://doi.org/10.1016/S2213-2600(20)30511-7

- *[Pre-print, not peer-reviewed]* Most SARS-CoV-2 serological assays were sensitive to interfering antibodies in samples from patients with chronic inflammatory diseases, which may lead to false positivity. Samples from patients with multiple sclerosis (MS), rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) were evaluated with 17 commercially-available lateral flow assays. Six of those assays, plus an in-house IgG assay, gave correct negative results, but 13 gave false positive results for patients with RA and SLE. Several assays had nonspecific signals for SARS-CoV-2 IgG or IgM for the majority of samples from patients with RA.

  > *Kharlamova et al. (Nov 13, 2020). SARS-CoV-2 Serological Tests Can Generate False Positive Results for Samples from Patients with Chronic Inflammatory Diseases. MedRxiv.* https://doi.org/10.1101/2020.11.13.20231076

Clinical Characteristics and Health Care Setting

- A retrospective analysis of adult emergency department visits from New York City found there may be populations of patients at high risk for COVID-19 who present with atypical complaints and symptoms. While most people who received SARS-CoV-2 testing had a fever, shortness of breath, or a cough, many others who received testing reported symptoms of weakness/falls/altered mental status (57.5%), poor glycemic control (55.5%), and gastrointestinal symptoms (51.4%). Among patients over 65, 76.7% of patients who had diarrhea, 73.7% with fatigue, and 69.3% reporting feeling weak had COVID-19. Among patients who died, 45.5% experienced dehydration, 40.5% had altered mental status, 27% had falls, and 24.6% had hyperglycemia.

  > *Clifford et al. (Nov 2020). Association between COVID-19 Diagnosis and Presenting Chief Complaint from New York City Triage Data. The American Journal of Emergency Medicine.* https://doi.org/10.1016j.ajem.2020.11.006

- A systematic review and meta-analysis comparing the frequency of gastrointestinal symptoms among COVID-19 patients from Chinese studies conducted earlier in the epidemic and more recent studies predominantly conducted outside of China found higher rates of diarrhea, nausea/vomiting, and abdominal pain in non-Chinese studies. The pooled prevalence estimate of any GI symptom was 0.21, and the most commonly reported symptoms were loss of appetite (18%) and diarrhea (15%). Studies that reviewed only inpatients found a lower prevalence of abdominal pain than studies that included outpatients only, or studies with both inpatients and outpatients.

  > *Akin et al. (Nov 10, 2020). Newly Reported Studies on the Increase in Gastrointestinal Symptom Prevalence With COVID-19 Infection: A Comprehensive Systematic Review and Meta-Analysis. Diseases.* https://doi.org/10.3390/diseases8040041

- *[Pre-print, not peer-reviewed]* Loss of smell was a reliable predictor of SARS-CoV-2 seropositivity in a study that screened over 500 healthcare workers at a regional critical care center in the UK. While 45% of participants reported symptoms potentially consistent with COVID-19, the overall seroprevalence was 14%. There was a significant difference in seropositivity between staff in clinical and non-clinical roles (9% patient facing critical care, 15% patient facing non-critical care, 22% not

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patient facing), which the authors note could be a result of stricter adherence to PPE guidelines in critical care settings. Among seropositive individuals, symptom severity increased with age for men but not for women, and there was no relationship between symptom severity and age or sex in the seronegative cohort who reported symptoms.

Baxendale et al. (Nov 13, 2020). Critical Care Workers Have Lower Seroprevalence of SARS-CoV-2 IgG Compared with Non-Patient Facing Staff in First Wave of COVID19. MedRxiv. https://doi.org/10.1101/2020.11.12.20145318

- A case of fetal death associated with intrauterine transmission of SARS-CoV-2 was documented in Brazil. SARS-CoV-2 RNA was detected in cotyledon samples, membranes, and umbilical cord blood aspirate, suggesting possible breakdown of the placental barrier. However, all fetal tissue samples tested negative. Examination and autopsy found placental lesions and vascular malperfusions, microglial hyperplasia, and lymphocytic infiltrate in muscle in the placenta and fetal tissue.

    Stonoga et al. (Feb 2021). Intrauterine Transmission of SARS-CoV-2. Emerging Infectious Diseases. https://doi.org/10.3201/eid2702.203824

Vaccines and Immunity

- *[Press release, not peer-reviewed]* The COVID-19 vaccine candidate (mRNA-1273) from Moderna demonstrated 94.5% efficacy in Phase 3 of the COVE study, which is evaluating the effect of the vaccine on disease prevention and severity. Interim results were based on 95 COVID-19 cases, 90 of which were reported in the placebo group and 5 in the vaccine group. 11 COVID-19 cases were severe, all of which occurred in the placebo group. Adverse events such as fatigue, injection site pain, and myalgia tended to be mild or moderate and resolved quickly.
    [Press release, not peer-reviewed] https://www.businesswire.com/news/home/20201116005608/en/Moderna's-COVID-19-Vaccine-Candidate-Meets-its-Primary-Efficacy-Endpoint-in-the-First-Interim-Analysis-of-the-Phase-3-COVE-Study

- *[Pre-print, not peer-reviewed]* A longitudinal study of sera from 308 SARS-CoV-2 RT-PCR positive individuals found that males exhibited a faster decline in anti-S and neutralizing antibodies than females, suggesting that the duration of protection may differ by sex. Higher levels of antibodies were observed one month after symptom onset among males, people over age 50, and those with a BMI >25. At months 3-6, while anti-S antibodies persisted in 99% of people, anti-N IgG antibodies were only found in 59% of people. Neutralizing antibody titers decreased twice as fast as anti-S IgG.
    Grzelak et al. (Nov 15, 2020). Sex Differences in the Decline of Neutralizing Antibodies to SARS-CoV-2. MedRxiv. https://doi.org/10.1101/2020.11.12.20230466

Mental Health and Personal Impact

- Job insecurity was associated with significant mental health burden among US young adults during the COVID-19 pandemic. An analysis of data from the weekly Household Pulse Survey from the US Census Bureau collected in June 2020 indicated that 59% of respondents (n=4,852) aged 18 to 26 experienced direct or household employment loss since the start of the pandemic, and 38% expected to experience employment loss in the subsequent four weeks. There were statistically significant associations between recent employment loss or expected employment loss and symptoms of poor mental health on all four measures in the study.
    Ganson et al. (Nov 2020). Job Insecurity and Symptoms of Anxiety and Depression Among U.S. Young Adults During COVID-19. Journal of Adolescent Health. https://doi.org/10.1016/j.jadohealth.2020.10.008

- In a cross-sectional study conducted at a children's hospital in Connecticut, there was a 60.8% reduction in children presenting to emergency departments with mental health-related diagnoses during the early COVID-19 pandemic period compared to 2019. Black children were significantly less likely to present with a mental health condition than white children during the pandemic as opposed to the pre-pandemic study period (p = 0.002).

  Leff et al. (Nov 13, 2020). Changes in Pediatric Emergency Department Visits for Mental Health during the COVID-19 Pandemic: A Cross-Sectional Study. Clinical Child Psychology and Psychiatry. https://doi.org/10.1177/1359104520972453

Modeling and Prediction

- A modeling study that tested scenarios with varying levels of SARS-CoV-2 vaccine efficacy found that a vaccine with prophylactic efficacy of ≥70% could eliminate infection and prevent major outbreaks in scenarios where 80% of the population receives the vaccine. A vaccine with a lower efficacy could still control infection in a scenario with additional reduction in contacts. If the vaccine efficacy were 50%, 2.4 people would need to be vaccinated to prevent one new infection, 25.5 to avoid one case of severe disease, 32.2 to avoid one case of critical disease, and 65.1 to avoid one death. The authors also note that vaccinated individuals increasing their social contacts might lessen the impact of a vaccine. The model scenarios reflect the epidemiology of SARS-CoV-2 in China.

  Makhoul et al. (Nov 9, 2020). Epidemiological Impact of SARS-CoV-2 Vaccination: Mathematical Modeling Analyses. Vaccines. https://doi.org/10.3390/vaccines8040668

Public Health Policy and Practice

- The outcomes of out-of-hospital cardiac arrest (OHCA) were worse during the first weeks of the COVID-19 pandemic in the US than one year prior. Rates of return of spontaneous circulation were 18% lower overall than before the pandemic (aRR = 0.82), including in communities with low COVID-19 mortality. Rates of survival to discharge were also lower during the pandemic (6.8% versus 9.8%), primarily in communities with moderate to high COVID-19 mortality. The incidence of OHCA was higher in 2020 than in 2019, but largely in communities with high or very high COVID-19 mortality.

  Chan et al. (Nov 14, 2020). Outcomes for Out-of-Hospital Cardiac Arrest in the United States During the Coronavirus Disease 2019 Pandemic. JAMA Cardiology. https://doi.org/10.1001/jamacardio.2020.6210

- A study evaluating the readability of online information from Google search results related to COVID-19 found that only 17.2% of webpages were presented at a universally-readable level. The first 20 webpage URLs for searches for "COVID", "COVID-19", and "coronavirus" from multiple predominantly English-speaking countries were evaluated on several readability assessment tools. There was a significant difference in readability based on the site's information source, with public health and government organizations presenting the most readable material.

  Worrall et al. (Dec 13, 2020). Readability of Online COVID-19 Health Information: A Comparison between Four English Speaking Countries. BMC Public Health. https://doi.org/10.1186/s12889-020-09710-5

Other Resources and Commentaries

- [Neurological Manifestations Associated with COVID-19: a Multicentric Registry](#) – Clinical Microbiology and Infection (Nov 2020)
- [Navigating the Risks of Flying During COVID-19: A Review for Safe Air Travel](#) – Journal of Travel Medicine (Nov 2020)
- [What's next for COVID-19 apps? Governance and oversight](#) – Science Magazine (Nov 2020)
- [Migrant Status, Ethnicity and COVID-19: More Accurate European Data are Greatly Needed](#) – Clinical Microbiology and Infection (Nov 2020)
- [A Drive-through Simulation Tool for Mass Vaccination during COVID-19 Pandemic](#) – Healthcare (Nov 2020)
- [A Framework for Research Linking Weather, Climate and COVID-19](#) – Nature Communications (Nov 2020)
- [Characterization of Pre-Existing and Induced SARS-CoV-2-Specific CD8+ T cells](#) – Nature Medicine (Nov 2020)
- [Communication Tools to Support Advance Care Planning and Hospital Care During the COVID-19 Pandemic: A Design Process](#) – Joint Commission Journal on Quality and Patient Safety (Nov 2020)
- [Review on the Contamination of Wastewater by COVID-19 Virus: Impact and Treatment](#) – The Science of the Total Environment (Nov 2020)
- [Conduct of Clinical Trials in the Era of COVID-19: JACC Scientific Expert Panel](#) – Journal of the American College of Cardiology (Nov 2020)
- [Analysis of Genomic Distributions of SARS-CoV-2 Reveals a Dominant Strain Type with Strong Allelic Associations](#) – Proceedings of the National Academy of Sciences (Nov 2020)

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