Washington State Department of Health

2019-nCoV Literature Situation Report (Lit Rep)
July 23, 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

➢ **Residents in long-term care facilities in Ontario, Canada had a 13-fold higher risk of death from COVID-19 compared to community-living adults age 70 and older.** More

➢ **Across 9 countries, age-standardized COVID-19 case fatality was 1.9%. There was wide variation in unadjusted country-level case-fatality, ranging from 0.7% in Germany to 9.3% in Italy. Adjustment for the age distribution of cases explained 66% of the between-country variation.** More

➢ **Compared to clinician-collected nasopharyngeal swabs, unsupervised self-collected midnasal swabs had a sensitivity of 80.0% and a specificity of 97.9% for diagnosing SARS-CoV-2.** More

➢ **SARS-CoV-2 viruses with the G614 mutation have become more prevalent as the pandemic has progressed and cases with G614 viruses have been shown to shed more viral RNA compared to the original D614 virus identified among the first human cases in Wuhan, China.** More

Non-Pharmaceutical Interventions

• Callow et al. gauged opinion and behaviors regarding COVID-19 and the Maryland Governor's lifting of lockdown restrictions among a convenience sample of 242 older adults. They found that attitudes toward social isolation were affected by perceived benefits and barriers to social distancing measures, perceived severity of COVID-19, and political affiliation.

> *Callow et al. (July 22, 2020). Older Adults' Intention to Socially Isolate Once COVID-19 Stay-at-Home Orders Are Replaced With "Safer-at-Home" Public Health Advisories: A Survey of Respondents in Maryland. Journal of Applied Gerontology.*
> https://doi.org/10.1177/0733464820944704

Transmission

• Intergenerational relationships (e.g., cohabitation and contact between family members of different generations) have been hypothesized to play a role in COVID-19 spread and case fatality. Using data from 19 European counties, Arpino et al. found that at the country level, higher levels of intergenerational relationships are associated with higher COVID-19 case fatality, although the magnitude of the association is small. At the subnational level, an opposite association is often observed. The authors advocate for policies that take into consideration the important instrumental and emotional support that intergenerational ties provide, which may increase compliance to the lockdown and "phase-2" restrictions.

> *Arpino et al. (July 22, 2020). No Clear Association Emerges between Intergenerational Relationships and COVID-19 Fatality Rates from Macro-Level Analyses. PNAS.*
> https://doi.org/10.1073/pnas.2008581117

- Korber et al. present evidence that SARS-CoV-2 viruses with the G614 mutation in the Spike protein are more prevalent than the original D614 form identified in the first human cases in Wuhan, China. In a follow-up study of 999 COVID-19 patients at the Sheffield Teaching Hospitals, patients infected with G614 shed more viral nucleic acid compared with those with D614 (p=0.037), and G614-viruses show significantly higher infectious titers in vitro than their D614 counterparts (2.6- to 9.3-fold increase, p<0.0001).

  Korber et al. (August 20, 2020). Tracking Changes in SARS-CoV-2 Spike: Evidence That D614G Increases Infectivity of the COVID-19 Virus. Cell. https://doi.org/10.1016/j.cell.2020.06.043

Testing and Treatment

- Compared to clinician-collected swabs, home-based self-collected swabs had a sensitivity of 80.0% (95% CI: 63-91%) and a specificity of 97.9% (95% CI: 94-99.5%). These results were based on a cohort of 185 symptomatic people who presented at drive-through clinics in Washington State who underwent both an unsupervised home self-collected swab and a clinician-collected nasopharyngeal swabs for diagnosis of SARS-CoV-2 infection by RT-PCR.

  McCulloch et al. (July 22, 2020). Comparison of Unsupervised Home Self-Collected Midnasal Swabs With Clinician-Collected Nasopharyngeal Swabs for Detection of SARS-CoV-2 Infection. JAMA Network Open. https://doi.org/10.1001/jamanetworkopen.2020.16382

- A review of 9 studies (293 total samples) found no statistically significant difference in viral loads between saliva, nasopharyngeal, or sputum specimens obtained for the detection of SARS-CoV-2. The authors suggest that these findings indicate that self-collected saliva may be a reliable and non-invasive approach for the detection of SARS-CoV-2 using RT-PCR.

  Fakheran et al. (July 15, 2020). Saliva as a Diagnostic Specimen for Detection of SARS-CoV-2 in Suspected Patients: A Scoping Review. Infectious Diseases of Poverty. https://doi.org/10.1186/s40249-020-00728-w

- TMPRSS2 is a cellular protease gene that activates SARS-CoV-2 for entry into lung cells. Hoffmann et al. report that the engineered expression of TMPRSS2 in *ex-vivo* Vero cells renders SARS-CoV-2 infection insensitive to chloroquine. Moreover, chloroquine did not block SARS-CoV-2 infection in TMPRSS2-positive lung cells. The authors conclude results indicate that chloroquine targets a pathway for viral activation that is not operative in lung cells and is unlikely to protect against SARS-CoV-2 spread in and between patients.

  Hoffmann et al. (July 22, 2020). Chloroquine Does Not Inhibit Infection of Human Lung Cells with SARS-CoV-2. Nature. https://doi.org/10.1038/s41586-020-2575-3

- Ramiro et al. evaluated clinical records of 86 patients with severe COVID-19-associated cytokine storm syndrome who received an intensive course of glucocorticoids. Compared to an untreated historical group of patients who received supportive care only (1:1 match on sex and age), treated patients had a higher rate of reaching respiratory recovery (HR=1.8), were less likely to die (HR=0.35), and had a lower rate of invasive mechanical ventilation (HR=0.29).

  Ramiro et al. (July 20, 2020). Historically Controlled Comparison of Glucocorticoids with or without Tocilizumab versus Supportive Care Only in Patients with COVID-19-Associated Cytokine Storm Syndrome: Results of the CHIC Study. Annals of the Rheumatic Diseases. https://doi.org/10.1136/annrheumdis-2020-218479

Clinical Characteristics and Health Care Setting

- Based on a cohort study among 627 long-term care (LTC) facilities in Ontario, Canada, the incidence of deaths related to COVID-19 was 13-fold higher among LTC residents compared to adults older than 69 years living in the community. This excess risk increased from 8-fold to 87-fold between March 29 and April 11. Infection among LTC staff was associated with death among residents with a 6-day lag.

  Fisman et al. (July 22, 2020). Risk Factors Associated With Mortality Among Residents With Coronavirus Disease 2019 (COVID-19) in Long-Term Care Facilities in Ontario, Canada. JAMA Network Open. https://doi.org/10.1001/jamanetworkopen.2020.15957

- In a cross-sectional study using population-based data on COVID-19 cases and deaths in 9 countries, Sudharsanan et al. observed an overall large variation in case-fatality. The highest case-fatality was reported in Italy (9.3%), and the lowest in Germany (0.7%). Adjustment for the age distribution of cases explains 66% of the between-country variation. The resulting age-standardized median case fatality was 1.9%. The authors conclude that it is important to focus on age-adjusted case fatality when comparing performance in caring for patients with COVID-19 and for monitoring the epidemic over time.

  Sudharsanan et al. (July 22, 2020). The Contribution of the Age Distribution of Cases to COVID-19 Case Fatality Across Countries: A 9-Country Demographic Study. Annals of Internal Medicine. https://www.acpjournals.org/doi/10.7326/m20-2973

- Based on data from the 2018 Behavioral Risk Factor Surveillance System (BRFSS) survey, the median county prevalence of any of five underlying medical conditions (chronic obstructive pulmonary disease, heart disease, diabetes, chronic kidney disease, and obesity) that are associated with increased risk for severe COVID-19 disease was 47% across 3,142 U.S. counties. While the total number of those with co-morbidities follows the overall population distribution, the prevalence of co-morbidities is higher in the southeastern United States and in more rural counties. County-level maps are provided to support local decision-makers in identifying areas at higher risk for severe COVID-19 illness.

  Razzaghi et al. (July 24, 2020). Estimated County-Level Prevalence of Selected Underlying Medical Conditions Associated with Increased Risk for Severe COVID-19 Illness — United States, 2018. Morbidity and Mortality Weekly Report 2020;69:945–950. http://dx.doi.org/10.15585/mmwr.mm6929a1

Modeling and Prediction

- *[Preprint, not peer reviewed]* Steyn et al. predicted the risk of undetected COVID-19 cases within managed isolation and quarantine facilities and the risk of infectious cases being released into the community using data during a two-week period (June 23 to July 6, 2020) in New Zealand.

- Under the current 14-day quarantine order, a combination of testing on days 3 and 12, daily symptom checks, and complete isolation of confirmed cases would reduce the risk of releasing an infectious case to an estimated 0.1% per arriving case. Shorter quarantine periods or reliance on testing only with no quarantine substantially increased the predicted risk. The ratio of cases detected on day 3 versus day 12 could be an effective indicator of the level of transmission.

  Steyn et al. (July 22, 2020). The Effect of Border Controls on the Risk of COVID-19 Reincursion from International Arrivals. Pre-print downloaded July 23 from https://doi.org/10.1101/2020.07.15.20154955

- Adekunle et al. estimated that there was a 79% reduction in imported COVID-19 cases in Australia as of March 2, 2020 and a one-month delay in the COVID-19 outbreak that was attributable to the travel bans imposed on January 24, 2020. Their model results aligned with the observed imported cases in Australia.

  Adekunle et al. (July 22, 2020). Delaying the COVID-19 Epidemic in Australia: Evaluating the Effectiveness of International Travel Bans. Australian and New Zealand Journal of Public Health. https://doi.org/10.1111/1753-6405.13016

Immunity

- A large number of monoclonal antibodies that potently neutralize the SARS-CoV-2 virus were identified from COVID-19 cases from New York. Liu et al. report the isolation of 61 SARS-CoV-2-neutralizing monoclonal antibodies from 5 infected patients hospitalized with severe disease at the Columbia University Irving Medical Center in New York City. Among these are 19 antibodies that potently neutralized the authentic SARS-CoV-2 virus *in vitro*, 9 of which exhibited exquisite potency. Epitope mapping show these antibodies are directed to the top of the viral spike, which the authors say indicates immunogenicity. Several of these monoclonal antibodies are promising candidates for clinical development as potential therapeutic and/or prophylactic agents against SARS-CoV-2.

  Liu et al. (July 22, 2020). Potent Neutralizing Antibodies Directed to Multiple Epitopes on SARS-CoV-2 Spike. Nature. https://doi.org/10.1038/s41586-020-2571-7

- *[Preprint, not peer reviewed]* The receptor-binding domain of the CoV spike (RBD-S) protein is important in host cell recognition and infection, and antibodies targeting this domain are often neutralizing. Graham et al. tested anti-RBD-S responses among 32 COVID-19 patients. They found that IgG, IgM, and IgA responses were all induced within 10 days following symptom onset, and IgG response was sustained over a 5-week period. No differences in responses were observed by age or sex, indicating that age-and sex-related disparities in COVID-19 fatality are not explained by anti-RBD-S responses. The authors concluded that the multi-isotype anti-RBD-S response could serve as a potential marker by which to monitor vaccine-induced responses.

  Graham et al. (July 22, 2020). Kinetics and Isotype Assessment of Antibodies Targeting the Spike Protein Receptor Binding Domain of SARS-CoV-2 In COVID-19 Patients as a Function of Age and Biological Sex. Pre-print downloaded July 23 from https://doi.org/10.1101/2020.07.15.20154443

Public Health Policy and Practice

- A group of experts from the Spanish Association of Sexuality and Mental Health released consensus recommendations to maintain lower-risk sexual activity during the COVID-19 pandemic. Specific recommendations include returning to engaging in safe sex for those with a stable partner after quarantine is over (28 to 33 days depending age) and if all parties are asymptomatic. Abstinence is recommended for those under quarantine, those with some clinical symptoms, health professionals in contact with COVID-19 patients, and during pregnancy. For persons without a partner, it is strongly recommended to not initiate sexual activity with a sporadic partner.

  Cabello et al. (July 20, 2020). Consensus on Recommendations for Safe Sexual Activity during the COVID-19 Coronavirus Pandemic. Journal of Clinical Medicine. https://doi.org/10.3390/jcm9072297

Other Resources and Commentaries

- Are We Responsible for the Racial Inequalities of Covid-19? – BMJ (July 22)

- [Covid-19 and Health Equity — Time to Think Big](#) – New England Journal of Medicine (July 22)
- [Serosurveillance and the COVID-19 Epidemic in the US](#) – JAMA (July 21)
- [A Simple Correction for Covid-19 Testing Bias](#) – ArXiv (July 15)
- [Structural Racism, Social Risk Factors, and Covid-19 — A Dangerous Convergence for Black Americans](#) – New England Journal of Medicine (July 22)
- [Opinion: It's Ethical to Test Promising Coronavirus Vaccines against Less-Promising Ones](#) – PNAS (July 22)
- [Age Is Just a Number: A Critically Important Number for COVID-19 Case Fatality](#) – Annals of Internal Medicine (July 22)
- [Planning for the Post-COVID Syndrome: How Payers Can Mitigate Long-Term Complications of the Pandemic](#) – Journal of General Internal Medicine (July 22)
- [COVID-19 and Persons with Substance Use Disorders: Inequities and Mitigation Strategies](#) – Substance Abuse (July 22)
- [ADHD as a Risk Factor for Infection With Covid-19](#) – Journal of Attention Disorders (July 22)
- [Transmission Route and Introduction of Pandemic SARS-CoV-2 between China, Italy and Spain](#) – Journal of Medical Virology (July 22)
- [On the Efficacy of Online Drug Surveys during the Time of COVID-19](#) – Substance Abuse (July 22)
- [Pooling Data From Individual Clinical Trials in the COVID-19 Era](#) – JAMA (July 22)
- [Point-of-Use Rapid Detection of SARS-CoV-2: Nanotechnology-Enabled Solutions for the COVID-19 Pandemic](#) – International Journal of Molecular Sciences (July 20)
- [Universal Screening for the SARS-CoV-2 Virus on Hospital Admission in an Area with Low COVID-19 Prevalence](#) – Infection Control & Hospital Epidemiology (July 23)
- [Financial Toxicity After Hospitalization; Considerations in Coronavirus Disease 2019 Recovery](#) – Critical Care Medicine (Aug 17)
- [The Need to Balance Basic and Clinical Research with the Safety of the Research Environment and Personnel in the Time of COVID-19 in the United States](#) – Current Medical Research and Opinion (July 22)
- [The Need to Balance Basic and Clinical Research with the Safety of the Research Environment and Personnel in the Time of COVID-19 in the United States](#) – Current Medical Research and Opinion (July 22)
- [Rapid Scaling Up of Covid-19 Diagnostic Testing in the United States — The NIH RADx Initiative](#) – New England Journal of Medicine (July 22)