



2019-nCoV Literature Situation Report (Lit Rep)

May 4, 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

- **Repeated universal testing (for instance, via mailed home testing kits) with isolation of infectious individuals can reduce transmission sufficiently to halt the epidemic, even with a false negative test rate of up to 15%**
- **Age, cardiovascular disease, COPD, and smoking are positively associated with risk of death due to COVID-19, however ACE inhibitor usage is not; for angiotensin-receptor-blockers the association is positive but not significant**
- **A randomized controlled trial of remdesivir found no significant difference in time to clinical improvement**
- **Pooling up to 32 samples in RT-PCR testing can reduce reagent demands with minimal losses to test validity**
- **Almost 94% percent of a sample of COVID-19 patients in a Wuhan Hospital were antibody positive for IgM, IgG, or both**
- **Reinfections with endemic coronaviruses are not atypical and can occur multiple times within a >1 year time window.**
- **A cross sectional survey of the US population found 37% of respondents felt non-Pharmaceutical Interventions (NPIs) were inconvenient, but only 0.9% believed that NPIs would not reduce their personal risk of illness**

Non-Pharmaceutical Interventions

- Authors in Sweden demonstrate that identification and isolation of the majority of infectious individuals (including those who are asymptomatic) by testing the entire population, repeatedly (i.e., through home test kits submitted by mail), would yield $R_0 < 1$. False positives can be tolerated as this would simply result in unnecessary quarantine, and the authors model the impact of false negatives using both a standard epidemiological model (SIR) and a stochastic model built on a social network graph. This strategy is effective at any prevalence level, and the authors suggest this approach is cost-effective but do not appear to have done a formal cost-effectiveness analysis.

Taipale et al. (May 1, 2020). Population-Scale Testing Can Suppress the Spread of COVID-19. Pre-print downloaded May 4 from Medrxiv. <https://doi.org/10.1101/2020.04.27.20078329>

Transmission

- Previous studies have shown high levels of SARS-CoV-2 in swab and sputum samples from individuals with no or mild symptoms of COVID-19. The authors modeled the airborne concentration of SARS-CoV-2 in a room the size of a small office or examination room using data on the distribution of aerosol sizes in exhaled breath generated by coughing versus normal breathing (emission data). They found virus concentration to be high in a room with a coughing emitter, or a high emitter breathing normally, and concluded strict respiratory protection is needed when in the same room as a potential patient.

Riediker et al. (May 3, 2020). Estimation of SARS-CoV-2 Emissions from Non-Symptomatic Cases. Pre-print downloaded May 4 from Medrxiv.

<https://www.medrxiv.org/content/10.1101/2020.04.27.20081398v1>

- Galanti and Shaman demonstrate that reinfections with the same endemic coronaviruses (HKU1, 229E, NL63, and OC43) are not unusual within a >1 year time window. Analyzing data collected through proactive sampling (nasal swab and self-report) in NYC from fall 2016 to spring 2018, 12 out of the 191 participants experienced one or more reinfection, with time of reoccurrence ranging from 4 to 48 weeks. Reinfection was not associated with symptom severity, but was associated with belonging to the same family cluster.

Galanti and Shaman. (May 3, 2020). Direct Observation of Repeated Infections with Endemic

Coronaviruses. Pre-print downloaded May 4 from <https://doi.org/10.1101/2020.04.27.20082032>

Testing and Treatment

- Using medical records from 169 hospitals in Asia, Europe, and North America, from 8,910 COVID-19 patients with known discharge status, these authors found the following factors were positively associated with risk of death (i.e., higher value of the factor associated with higher risk of death): age >65 years, coronary artery disease, heart failure, cardiac arrhythmia, COPD, current smoking. Odds ratio were between 1.79 and 2.95 for all factors. For use of ACE inhibitors the association was negative, and for angiotensin-receptor-blockers the association was positive but not significant.

Mehra et al. (May 1, 2020). Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19.

The New England Journal of Medicine. <https://doi.org/10.1056/NEJMoa2007621>

- Use of hydroxychloroquine can increase the risk of corrected QT (QTc) prolongation, a type of cardiac arrhythmia. Among 90 patients in an academic tertiary care center in Boston with at least one positive test for SARS-CoV-2, QTc was significantly longer after initiation of hydroxychloroquine, and this effect stronger for patients receiving both hydroxychloroquine and azithromycin. The authors recommend judicious use of hydroxychloroquine, along with monitoring of QTc and concomitant medications.

Mercurio et al. (May 1, 2020). Risk of QT Interval Prolongation Associated With Use of Hydroxychloroquine With or Without Concomitant Azithromycin Among Hospitalized Patients Testing Positive for Coronavirus Disease 2019 (COVID-19). JAMA Cardiology.

<https://doi.org/10.1001/jamacardio.2020.1834>

- A randomized, double-blind, placebo controlled multicenter trial at ten hospitals in Hubei, China with 237 participants (158 randomized to remdesivir, 79 to placebo) demonstrated that time to clinical improvement did not differ by study arm, with 21 days (IQR 13-28 days) in the remdesivir

group versus 23 days (IQR 15-28 days) in the placebo group (HR 1.23, 95% CI 0.87 – 1.75). Overall frequency of adverse events was similar in both groups; however treatment cessation due to adverse events was higher in the remdesivir (12%) than placebo (5%) group.

Wang et al. (Apr 29, 2020). Remdesivir in Adults with Severe COVID-19 : A Randomised, double-blind, placebo-controlled, multicentre trial. The Lancet. [https://doi.org/10.1016/S0140-6736\(20\)31022-9](https://doi.org/10.1016/S0140-6736(20)31022-9)

- Many healthcare systems are experiencing shortages of reagents for SARS-CoV-2 diagnostic testing. These authors were able to detect a single positive sample in pools of up to 32 negative samples, either before or after RNA extraction, with an estimated false negative rate of 10%. Single positive samples could also be recovered from pools of 64 (the highest pool size tested) with additional amplification cycles. Pooled testing could be applied immediately to expand screening capacities.

Yelin et al. (May 2, 2020). Evaluation of COVID-19 RT-QPCR Test in Multi-Sample Pools. Clinical Infectious Diseases. <https://doi.org/10.1093/cid/ciaa531>

- Using CHO cell expressed full length SARS-CoV-2 S1 protein as capturing antigen, Zhao et al. develop and validate a rapid COVID-19 serology ELISA kit able to detect SARS-CoV-2 antibody 1 day after the onset of COVID-19. The reported specificity and sensitivity of the ELISA kit was 97.5% and 97.1%, respectively, with overall accuracy rate of 97.3% (based on 412 negative and 69 positive samples). Rapid serological tests such as these could contribute to additional surveillance in hospitals and other frontline environments where there is a high volume of close contact with confirmed cases.

Zhao et al. (May 1, 2020). Early Detection of SARS-CoV-2 Antibodies in COVID-19 Patients as a Serologic Marker of Infection. Clinical Infectious Diseases. <https://doi.org/10.1093/cid/ciaa523>

Clinical Characteristics and Health Care Setting

- Antibody tests designed to detect envelope protein E and nucleocapsid protein N were conducted on 112 COVID-19 (PCR positive) patients admitted to a hospital in Wuhan, China in February 2020. One hundred and five (93.8%) were positive for either IgM, IgG, or both. Timing of testing with respect to disease onset varied, and was less than 10 days (i.e., possibly prior to antibody production) for 7 participants (two of whom were negative to both IgM and IgG). IgM and IgG titers did not differ between those who were PCR negative versus positive after treatment.

Zhang et al. (May 2, 2020). Longitudinal Change of SARS-Cov2 Antibodies in Patients with COVID-19. The Journal of Infectious Diseases. <https://doi.org/10.1093/infdis/jiaa229>

Mental Health and Personal Impact

- Blake et al. present a free digital learning package to mitigate the impacts of COVID-19 on the mental health of healthcare workers. The e-package was designed through an agile methodology consisting of public involvement activities and content and technical development with iterative peer review. It outlines actions for team leaders, guidance on communication and reducing social stigma, self-care strategies, and managing emotions.
- Evaluation indicated high user satisfaction and has already been highly accessed and adopted by various healthcare providers within their health and wellbeing provisions.

Blake et al. (Apr 26, 2020). Mitigating the Psychological Impact of COVID-19 on Healthcare Workers: A Digital Learning Package. International Journal of Environmental Research and Public Health. <https://doi.org/10.3390/ijerph17092997>

Modeling and Prediction

- Arneson et al. report on the development of CovidCounties.org, an interactive web-based application that depicts daily disease trends at the US county level. Accompanying the application is a manually curated data set of all major public policy actions at the state level. Data for the website was primarily derived from The New York Times, the US Census, and Kaiser Health News. Manually curated data were obtained from the websites of multiple state departments of health.
- Data and tools incorporated into CovidCounties support the effectiveness of social distancing.
- The code for CovidCounties is available open source, unlike other COVID-19 dashboards.

Arneson et al. (May 2, 2020). CovidCounties - an Interactive Real-Time Tracker of the COVID-19 Pandemic at the Level of US Counties. Pre-print downloaded May 4 from <https://doi.org/10.1101/2020.04.28.20083279>

- Keskinocak et al. develop an agent-based simulation model populated using COVID-19 specific parameters and data from Georgia on agent's interactions and demographics. The simulation covered a 6-month period and tested different social distancing scenarios and a combination of shelter-in-place and voluntary quarantine with varying timelines and compliance levels.
- The combined interventions of shelter-in-place followed by voluntary quarantine both delayed and reduced the peak infection by up to 3 months and by 40%. Regardless of shelter-in-place duration, increasing voluntary quarantine compliance can decrease cumulative infection rate by 50%.

Keskinocak et al. (May 3, 2020). The Impact of Social Distancing on COVID19 Spread State of Georgia Case Study. Pre-print downloaded May 4 from <https://doi.org/10.1101/2020.04.29.20084764>

Public Health Policy and Practice

- Kantor and Kantor performed a national cross sectional survey (N=1005) of the general US population on beliefs, attitudes, and actions regarding non-pharmaceutical interventions (NPIs). While 37% felt that NPIs were inconvenient, only 0.9% believed that NPIs would not reduce their personal risk of illness. NPI adherence was associated with belief that NPI would reduce personal risk of illness (OR 3.06) and belief that they were not difficult to perform (OR 1.79).
- Results show a higher degree of compliance to straightforward NPI recommendations, such as handwashing, compared with more onerous approaches such as masking and disinfecting surfaces.

Kantor and Kantor. (May 1, 2020). Nonpharmaceutical Interventions for Pandemic COVID-19 A Cross-Sectional Investigation of US General Public Beliefs Attitudes and Actions. Pre-print downloaded May 4 from <https://doi.org/10.1101/2020.04.26.20078618>

Other Resources and Commentaries

- [Consideration of the Aerosol Transmission for COVID-19 and Public Health](#) – Risk Analysis (May 3)
- [How the COVID-19 pandemic is favoring the adoption of digital technologies in healthcare a rapid literature review](#) – Pre-print (May 4)
- [The Business of Medicine in the Era of COVID-19](#) – JAMA (May 1)
- [COVID-19: Therapeutics and Their Toxicities](#) – Journal of Medical Toxicology (May 3)

This report was prepared by the UW MetaCenter for Pandemic Preparedness and Global Health Security in collaboration with and on behalf of WA DOH COVID-19 Incidence Management Team