



## 2019-nCoV Literature Situation Report (Lit Rep)

April 21, 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

- ❑ **Multiple studies evaluate the effectiveness of non-pharmaceutical interventions. While border closures, quarantine policies and business closures were generally associated with reduced SARS-CoV-2 (and, in one study, influenza) transmission, school closures were noted as the least effective intervention.**
- ❑ **Qian et al present highly sensitive IgG and IgM serological assay testing for SARS-CoV-2. This may add value when combined with nucleic acid testing (RT-PCR), which shows increasing evidence of false-negative results in other studies.**
- ❑ **Diarrhea in COVID-19 patients may be a risk factor for presence of viral RNA in stool as well as prolonged viral shedding.**
- ❑ **Positive viral RNA presence in fecal and sputum samples from discharged patients highlights the need for increased follow-up among discharged patients.**

### Non-Pharmaceutical Interventions

- The authors provide estimates on the effectiveness of various non-pharmaceutical interventions based on early estimates from 20 countries, including the US.
- Closure of venues was associated with a 33% reduction in new cases (95% CI: 16-47%), bans on non-essential business with a 28% reduction (10-42%), border closures with a 26% reduction (13-37%), and school closures only 11% (0-27%). These findings are relevant for evaluating current containment policies.

*Banholzer et al. (April 21, 2020). The estimated impact of non-pharmaceutical interventions on documented cases of COVID-19: A cross-country analysis. Pre-print downloaded Apr 21 from <https://doi.org/10.1101/2020.04.16.20062141>*

- The authors assess the effectiveness of travel restrictions in Wuhan on delaying or reducing transmission of COVID-19 to other major cities in China. They conclude that restrictions alone did not have a substantial impact, as local transmission in other cities had already been occurring prior to implementation.

*Quilty et al. (April 21, 2020). The effect of inter-city travel restrictions on geographical spread of COVID-19: Evidence from Wuhan, China. Pre-print downloaded Apr 21 from <https://doi.org/10.1101/2020.04.16.20067504>*

- The authors analyzed data on influenza and coronavirus transmission in response to non-pharmaceutical interventions implemented in Hong Kong. COVID-19 transmission has slowed, with an  $R_1$  (transmission rate per case) of  $\sim 1$  sustained for 8 weeks, and influenza community transmission has been reduced by 44%, with a 33% reduction in pediatric hospitalization rates.
- This study shows that NPIs such as border restrictions, quarantine and isolation, and social distancing are associated with reduced COVID-19 transmission, and are also likely to reduce influenza transmission.

*Cowling et al. (April 17, 2020). Impact assessment of non-pharmaceutical interventions against coronavirus disease 2019 and influenza in Hong Kong: an observational study. Lancet Public Health. [https://doi.org/10.1016/S2468-2667\(20\)30090-6](https://doi.org/10.1016/S2468-2667(20)30090-6)*

## Transmission

- This epidemiological and genomic analysis from 10 patients in Shaoxing led to an estimated average mutation rate of  $1.37 \times 10^{-3}$  nucleotide substitution per site per year, similar to other coronaviruses.
- The authors conclude that the moderate mutation rate lends hope to the development of an effective long-lasting vaccine.

*Chen et al. (April 21, 2020). Epidemiological and Genomic Analysis of SARS-CoV-2 in Ten Patients from a Mid-sized City outside of Hubei, China. Pre-print downloaded Apr 21 from <https://doi.org/10.1101/2020.04.16.20058560>*

## Geographic Spread

- This analysis of 156 SARS-CoV-2 sequences from New York City showed that most samples were related to viral outbreaks in Europe, and suggest numerous seed transmissions and a period of unrecognized community spreading.

*Maurano et al. (April 21, 2020). Sequencing analysis of the spread of SARS-CoV2 in the Greater New York City Region. Pre-print downloaded Apr 21 from <https://doi.org/10.1101/2020.04.15.20064931>*

## Testing and Treatment

- Qian et al evaluated the clinical sensitivity of IgM and IgG SARS-CoV-2 antibody testing using 972 non-COVID-19 patients, 586 normal donors, and 503 RT-PCR-confirmed cases.
- IgM and IgG show clinical sensitivity of 85.88% and 96.62% respectively for confirmed SARS-Cov-2 infection with RT-PCR. These assays may add great value to nucleic acid testing.

*Qian et al. (April 21, 2020). Development and Multicenter Performance Evaluation of The First Fully Automated SARS-CoV-2 IgM and IgG Immunoassays. Pre-print downloaded Apr 21 from <https://doi.org/10.1101/2020.04.16.20067231>*

- Arevalo-Rodriguez et al reviewed available evidence on false-negative RT-PCR results when testing for SARS-CoV-2 using 5 studies enrolling 957 patients in total.
- While cautious in interpretation due to potential bias and heterogeneity of findings, the authors report the pooled false-negative proportion of 0.085 (95% CI= 0.034-0.196) and reinforce the need for repeated testing in patients with suspicion of SARS-CoV-2 infection.

*Arevalo-Rodriguez et al. (April 21, 2020). False-Negative Results of Initial RT-PCR Assays for COVID-19: A Systematic Review. Pre-print downloaded Apr 21 from <https://doi.org/10.1101/2020.04.16.20066787>*

- This retrospective analysis of 368 patients who had received hydroxychloroquine (with azithromycin or alone) explored the association between treatment and the primary outcomes of mechanical ventilation and death.
- No evidence was found of reduced risk of mechanical ventilation, and use of hydroxychloroquine alone was associated with an increased risk of overall mortality. These findings highlight the importance of randomized controlled study results before widespread adoption of these drugs.  
*Magagnolia et al. (April 21, 2020). Outcomes of hydroxychloroquine usage in United States veterans hospitalized with Covid-19. Pre-print downloaded Apr 21 from <https://doi.org/10.1101/2020.04.16.20065920>*
- The authors report positive rates of COVID-19 tests based on nucleic acid testing, chest CT, and serological antibody tests in Wuhan, observing a 10% SARS-CoV-2 specific IgG positive rate from 1,402 tests.
- Combination of nucleic acid and serological testing might facilitate the detection of COVID-19 infection.  
*Wu et al. (April 20, 2020). Serological tests facilitate identification of asymptomatic SARS-CoV-2 infection in Wuhan, China. J Med Virol. <https://doi.org/10.1002/jmv.25904>*

### Clinical Characteristics and Health Care Setting

- The authors evaluated the performance of the Modified Early Warning Score (MEWS) and Rapid Emergency Medicine Score (REMS) when applied to 138 critically ill COVID-19 patients.
- REMS was a better predictor of mortality among both age groups (<65 and 65+ years old), and could provide emergency clinicians with an effective adjunct risk stratification tool for critically ill patients.  
*Hu et al. (April 20, 2020). Comparing rapid scoring systems in mortality prediction of critical ill patients with novel coronavirus disease. Acad Emerg Med. <https://doi.org/10.1111/ACEM.13992>*
- This retrospective analysis of 84 patients with SARS-CoV-2 pneumonia in Wuhan found that duration of fever and shortness of breath in patients with diarrhea was significantly longer than those without, and that patients with diarrhea have a higher proportion of SARS-CoV-2 viral RNA detection in stool.  
*Wei et al. (April 18, 2020). Diarrhea is associated with prolonged symptoms and viral carriage in COVID-19. Clin Gastroenterol Hepatol. <https://doi.org/10.1016/j.cgh.2020.04.030>*
- This study summarizes clinical data from four recent studies involving clinical characteristics of COVID-19 to determine the incidence of GI symptoms and explore the potential mechanism of diarrhea and other GI manifestations of disease.
- Results reveal that ACE mRNA and proteins are highly expressed in the small intestine, which may mediate the invasion and amplification of SARS-CoV-2 and activation of GI inflammation.  
*Zhang et al. (April 18, 2020). Specific ACE2 Expression in Small Intestinal Enterocytes may Cause Gastrointestinal Symptoms and Injury after 2019-nCoV Infection. Int J Infect Dis. <https://doi.org/10.1016/j.ijid.2020.04.027>*

### Public Health Policy and Practice

- Follow-up testing of 13 discharged COVID-19 patients revealed 2 patients continuously tested positive for SARS-CoV-2 even though sputum was negative, and 4 patients had positive sputum samples 5-14 days after discharge.

- Under present discharge criteria, the high presence of SARS-CoV-2 RNA indicates potential infectivity. The authors recommend adding a negative result from fecal testing to discharge criteria, and strengthening of follow-up procedures with discharged patients.  
*Li et al. (April 20, 2020). Positive result of Sars-Cov-2 in faeces and sputum from discharged patient with COVID-19 in Yiwu, China. J Med Virol. <https://doi.org/10.1002/jmv.25905>*
- This study monitored the presence of detectable SARS-Cov-2 among hospital environment surfaces, sewage, and PPE of staff in isolation wards. All 36 environmental and 9 PPE samples were negative. All 3 sewage samples from the inlet preprocessing pool were positive, however samples from the outlet of the last disinfection pool were negative.
- Findings suggest that strict disinfection and hand hygiene could decrease hospital-associated COVID-19 infection risk to staff working in isolation wards.  
*Wang et al. (April 18, 2020). SARS-CoV-2 RNA detection of hospital isolation wards hygiene monitoring during the Coronavirus Disease 2019 outbreak in a Chinese hospital. <https://doi.org/10.1016/j.ijid.2020.04.024>*

### Other Resources and Commentaries

- [Use of non-invasive ventilation for patients with COVID-19: a cause for concern?](#) – Lancet Respir (Apr 20)
- [COVID-19 during pregnancy: a systematic review of reported cases](#) – Am J Obstetr Gynecol (Apr 18)
- [Assessment of the quality of systematic reviews on COVID-19: A comparative study of previous coronavirus outbreaks](#) – J Med Virol (Apr 17)
- [COVID-19 admissions calculators: General population and paediatric cohort](#)—Early Human Develop (Apr 2020)
  - This paper presents an interactive spreadsheet model to estimate population and pediatric admissions for a given population, using Malta as an example.