

## 2019-nCoV Literature Situation Report (Lit Rep) February 26, 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

- **An analysis of publicly available data on COVID-19 mortality in England and Wales suggests that absolute mortality rates (all cause) for teachers were low, and that primary school teachers were not at elevated risk of death compared to the general population. Secondary school teachers had a slightly higher risk of dying of COVID-19 relative to all professionals and working-aged people.** [More](#)
- **In Israel, where 2-dose coverage with the Pfizer-BioNTech mRNA vaccine reached 84% among persons aged  $\geq 70$  years and 10% among those aged  $< 50$  years by February 2021, there was a 67% decline in the ratio of COVID-19 patients aged  $\geq 70$  years requiring mechanical ventilation to those aged  $< 50$  years. The authors conclude that this is preliminary evidence of the effectiveness of vaccines in preventing severe cases of COVID-19 at the national level.** [More](#)
- **Cross reactive antibodies generated by pre-pandemic human coronavirus (hCoV) infections are common but are not associated with protection against SARS-CoV-2 infection or with poor clinical outcomes after infection with SARS-CoV-2.** [More](#)

### Non-Pharmaceutical Interventions

- A higher number of symptoms and higher viral loads were associated with subsequent clusters of SARS-CoV-2 cases among cohorts of US Air Force basic trainees. Among 10,613 US Air Force basic trainees, of whom 3% (403) received a diagnosis of COVID-19 during the study period, higher numbers of symptoms and higher viral loads (lower cycle threshold (Ct) values) were associated with subsequent development of clusters of individuals with COVID-19 infection. The authors suggest that Ct values may be useful in assessing risk of ongoing transmission in specific cohorts.
- Although individual cases of COVID-19 occurred in almost half of all training cohorts, only 11% of cohorts had an initial individual case that resulted in a cluster of 5 or more cases, a success that the authors attributed to effective non-pharmaceutical interventions among the trainees.

*Marcus et al. (Feb 25, 2021). Risk Factors Associated With COVID-19 Transmission Among US Air Force Trainees in a Congregant Setting. JAMA Network Open.*

<https://doi.org/10.1001/jamanetworkopen.2021.0202>

### Testing and Treatment

- A multi-center phase 3 clinical trial of intravenous treatment using the IL-6 receptor antagonists tocilizumab in hospitalized patients with severe COVID-19 pneumonia found that tocilizumab did not result in significantly better clinical status or reduced mortality compared to placebo (19.7% vs

19.4%) at 28 days. At day 14, clinical status was also not to be significantly different between treatment and placebo. Time until hospital discharge (HR=1.36) was lower in the tocilizumab treatment group. In a population of patients monitored for safety, both adverse event and serious adverse events were similar between the treatment and placebo group (Adverse event: 77.3% vs 81.1%; serious adverse event: 34.9% vs. 38.5%). Only 19% of participant in the tocilizumab arm and 28.5% of participants in the placebo arm received glucocorticoids.

Rosas et al. (Feb 25, 2021). *Tocilizumab in Hospitalized Patients with Severe Covid-19 Pneumonia*. *New England Journal of Medicine*. <https://doi.org/10.1056/NEJMoa2028700>

- A trial of two IL-6 receptor antagonists, tocilizumab and sarilumab, in critically ill hospitalized adults with confirmed COVID-19 found that in-hospital mortality in the pooled IL-6 receptor antagonist groups was 27% (108 of 395 patients), as compared with 36% (142 of 397 patients) in the group of people receiving standard care, which results in a posterior probability of >99.5% that the treatments improved in-hospital survival. 93% of all patients were treated with glucocorticoids. Both drugs were effective across all secondary outcomes, including 90-day survival and time to ICU and hospital discharge.

Gordon et al. (Feb 25, 2021). *Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19*. *New England Journal of Medicine*. <https://doi.org/10.1056/NEJMoa2100433>

- [Pre-print, not peer-reviewed] An *in vitro* study of the neutralizing ability of the monoclonal antibody treatment bamlanivimab against five emerging SARS-CoV-2 variants of concern determined no neutralization effect could be detected against either the B.1.351 (first described in South Africa) or P.2 (first described in Brazil) variants, both of which harbor the E484K substitution. The antibody was able to efficiently neutralize the B.1.17 variant (first described in the UK), as well as isolates FFM1 and FFM7 from early 2020. These findings indicate screening for E484K substitutions may be needed before initiating monoclonal antibody treatment with bamlanivimab.
- Neutralizing effect of vaccine-elicited sera (following vaccination with the Pfizer-BioNTech COVID-19 Vaccine [BNT162b2]) and convalescent sera were also tested in the 5 variant strains. Vaccine-elicited sera showed neutralizing activity against FFM1 and FFM7, and slightly decreased activity against B1.1.7, B.1.351 and P.2. Convalescent sera showed lower neutralizing activity against B1.1.7, B.1.135 and P.2 compared to FFM1 and FFM7. [EDITORIAL NOTE: The manuscript refers to both B.1.351 and B.1.135. It is assumed that B.1.135 was a typographical error and B.1.351 was used throughout in this summary.]

Widera et al. (Feb 26, 2021). *Bamlanivimab Does Not Neutralize Two SARS-CoV-2 Variants Carrying E484K in Vitro*. Pre-print downloaded Feb 26 from <https://doi.org/10.1101/2021.02.24.21252372>

- In patients hospitalized with COVID-19, the administration of 6 mg/day for ten days of the steroid dexamethasone resulted in statistically significantly lower 28-day mortality among those who were receiving either invasive mechanical ventilation (29% vs. 41%) or oxygen alone (23% vs. 26%) at randomization but not among those receiving no respiratory support (18% vs. 14%). Patients in the dexamethasone group also had a shorter duration of hospitalization than those in the usual care group (median, 12 days vs. 13 days). [EDITORIAL NOTE: An earlier analysis of this RECOVERY trial was summarized as a pre-print on July 20, 2020.]

Horby et al. (July 17, 2020). *Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report*. *New England Journal of Medicine*. <https://doi.org/10.1056/NEJMoa2021436>

- A systematic review and meta-analysis of randomized trials published between the beginning of the pandemic and September 2020 found that ten days of remdesivir compared to standard care was associated with a lower risk of death in patients with COVID-19. The review, which covered 25 trials evaluating 17 treatments among a total of 11,597 patients, also found that a five-day course of remdesivir was associated with a higher frequency of clinical improvement compared to standard care, and that remdesivir for either five or ten days, lopinavir/ritonavir, and dexamethasone reduced the risk of any severe adverse events by 52% compared to standard care. Of all the drugs tested, colchicine and high doses of hydroxychloroquine raised the most safety concerns.

*Diallo et al. (Feb 3, 2021). An Updated Systematic Review and Network Meta-Analysis of 25 Randomized Trials Assessing the Efficacy and Safety of Treatments in COVID-19 Disease. Journal of Public Health Research. <https://doi.org/10.4081/jphr.2021.1945>*

- Parikh et al. suggest that “dry swabs” (which do not use transport medium) may be accurate for SARS-CoV-2 diagnostics. Flocked swabs were inoculated with SARS-CoV-2 and then incubated in either the typical medium or a dry, sterile conical tube. All dry swabs tested at days 1, 2, and 7 provided results that were within two cycle thresholds (Cts) of the average Ct values for swabs hydrated in the same media and tested on day 0. Not using transport media may alleviate supply shortfalls.

*Parikh et al. (Feb 25, 2021). The Effects of “Dry Swab” Incubation on SARS-CoV-2 Molecular Testing. The Journal of Applied Laboratory Medicine. <https://doi.org/10.1093/jalm/ifa010>*

## Vaccines and Immunity

- In Israel, the ratio of COVID-19 patients over the age of 70 requiring mechanical ventilation declined 67% compared to those under 50 from October–December 2020 to February 2021 after a national immunization program resulting in a 2-dose vaccination coverage of 84% among people over the age of 70. The authors suggest that this provides preliminary evidence that the nationwide vaccination campaign has been effective in reducing severe COVID-19 requiring mechanical ventilation.

*Rinott et al. (Feb 26, 2021). Reduction in COVID-19 Patients Requiring Mechanical Ventilation Following Implementation of a National COVID-19 Vaccination Program — Israel, December 2020–February 2021. MMWR. <https://doi.org/10.15585/mmwr.mm7009e3>*

- Cross reactive antibodies generated by pre-pandemic human coronavirus (hCoV) infections are common but are not associated with protection against infection or poor clinical outcomes after infection with SARS-CoV-2. Using samples from a pre-pandemic biobank, 4% of pre-pandemic sera contained antibodies that bound the full-length spike from SARS-CoV-2 and 16% of samples contained antibodies capable of binding SARS-CoV-2 nucleocapsid. Pre-pandemic serum containing these antibodies was wholly incapable of neutralizing SARS-CoV-2 in either pseudovirus or live virus assays. The baseline presence or absence of non-neutralizing cross-reactive antibodies was not associated with protection against SARS-CoV-2 infection or clinical outcomes after infection in a cohort of 251 participants who went on to develop SARS-CoV-2. Levels of some of these hCoV antibodies were boosted upon infection with SARS-CoV-2.

*Anderson et al. (Feb 9, 2021). Seasonal Human Coronavirus Antibodies Are Boosted upon SARS-CoV-2 Infection but Not Associated with Protection. Cell. <https://doi.org/10.1016/j.cell.2021.02.010>*

- *[pre-print; not peer-reviewed]* Levels of plasma SARS-CoV-2 viremia at the time of presentation to a hospital's emergency department predicted both disease severity and mortality within 28 days. Viremia (defined as presence of SARS-CoV-2 RNA in plasma samples) was present in around 40% of participants and was associated with a dose-dependent effect on clinical outcome.  
*Li et al. (Feb 26, 2021). SARS-CoV-2 Viremia Is Associated with Distinct Proteomic Pathways and Predicts COVID-19 Outcomes. Pre-print downloaded Feb 26 from <https://doi.org/10.1101/2021.02.24.21252357>*
- *[pre-print; not peer-reviewed]* Antibody titers two weeks after receiving a second dose of the Pfizer-BioNTech vaccine were lower in obese healthcare workers (BMI >30), after adjusting for age. 99.5% of the 248 participants developed a humoral immune response after vaccination, and antibody titers were higher in younger people and in women. The authors note that the importance of the magnitude of a humoral response is still under investigation.  
*Pellini et al. (Feb 26, 2021). Obesity May Hamper SARS-CoV-2 Vaccine Immunogenicity. Pre-print downloaded Feb 26 from <https://doi.org/10.1101/2021.02.24.21251664>*

## Modeling and Prediction

- *[Report, not peer-reviewed]* Covasim, a model previously used to describe SARS-CoV-2 transmission among inter-personal contacts in King County, Washington predicted that the rate of introduction of SARS-CoV-2 into K-12 school classroom settings is proportional to the prevalence of SARS-CoV-2 in the community. The model is an agent-based model of contacts at home, school, work and in the community. According to the model, each 0.1% increase in community prevalence resulted in an increase in daily introduction rate by 3.1 per 100,000 population. In a classroom setting, if in-school transmissibility is low, potential outbreaks were predicted to be small, with additional countermeasures such as asymptomatic testing adding little value. If transmission is high, however, large outbreaks are possible with more transmissible variants or if interventions are insufficient. The model also predicted that the frequency of exports from schools to the broader community is dependent on the number of students infected in the schools.  
*Klein et al. (2021). Stepping Back to School: A Step-by-Step Look at COVID Introduction, Spread, and Exportation. [https://covid.idmod.org/data/Stepping\\_Back\\_to\\_School.pdf](https://covid.idmod.org/data/Stepping_Back_to_School.pdf)*
- *[Pre-print, not peer-reviewed]* An agent-based model estimated the impact of a strategy of delaying a second COVID-19 vaccine dose on cumulative mortality and found that a delayed second dose approach could result in reduced cumulative mortality under certain conditions, particularly in people under 65 years of age. The model was constructed using a simulated population of 100,000 agents based on a real-world US county. It predicted both a reduction in total mortality and cumulative infections at assuming and 80% and 90% first dose efficacy, resulting in absolute cumulative mortality reductions between 26 and 47 deaths per 100,000 population. The model also suggested that a delayed second dose for people under 65 years of age is optimal, assuming a first-dose efficacy of 80% and for vaccination rates at or below 0.3% population per day. The conditions in which these reductions were observed included the first dose efficacy being above 70% and vaccination rates remaining below 1% of the population per day.  
*Romero-Brufau et al. (Feb 26, 2021). The Public Health Impact of Delaying a Second Dose of the BNT162b2 or MRNA-1273 COVID-19 Vaccine. Pre-print downloaded Feb 26 from <https://doi.org/10.1101/2021.02.23.21252299>*

## Public Health Policy and Practice

- *[pre-print; not peer-reviewed]* An analysis of publicly available data on COVID-19 mortality in England and Wales suggests that absolute mortality rates for teachers were low (under 39 per 100,000), but that secondary school teachers had slightly higher risk of dying of COVID-19 relative to all professionals and working-aged people. Primary school teachers were not at elevated risk of death compared to the general population. Excess deaths were higher in teachers over the age of 65 when compared to all people over 65, although COVID-19 was implicated in only 35% of those cases. Lewis et al. (Feb 26, 2021). *Risk of Death among Teachers in England and Wales during the Covid19 Pandemic*. Pre-print downloaded Feb 26 from <https://doi.org/10.1101/2021.02.23.21252143>

## Other Resources and Commentaries

- [Tracking Coronavirus Cases at U.S. Colleges and Universities](#) – The New York Times (Feb 25)
- [The Benefits of Vaccinating With the First Available COVID-19 Coronavirus Vaccine](#) – American Journal of Preventive Medicine (Jan 18)
- [SARS-CoV-2: A Systematic Review of Indoor Air Sampling for Virus Detection](#) – Environmental Science and Pollution Research (Feb 25)
- [Impact of the Influenza Vaccine on COVID-19 Infection Rates and Severity](#) – American Journal of Infection Control (Feb 22)
- [Public Health Decisions in the COVID-19 Pandemic Require More than ‘Follow the Science’](#) – Journal of Medical Ethics (Feb 25)
- [How Vulnerable Are U.S. Crop Workers?: Evidence from Representative Worker Data and Implications for COVID-19](#) – Journal of Agromedicine (Feb 25)
- [Vaccinating the Oldest against COVID-19 Saves Both the Most Lives and Most Years of Life](#) – Proceedings of the National Academy of Sciences (Jan 28)
- [Announcing the Lancet Commission on Vaccine Refusal, Acceptance, and Demand in the USA](#) – The Lancet (Feb 26)
- [Difference in SARS-CoV-2 Attack Rate between Children and Adults May Reflect Bias](#) – Clinical Infectious Diseases (Feb 26)
- [Interleukin-6 Receptor Inhibition in Covid-19 — Cooling the Inflammatory Soup](#) – New England Journal of Medicine (Feb 25)
- [Modelling Suggests Limited Change in the Reproduction Number from Reopening Norwegian Kindergartens and Schools during the COVID-19 Pandemic](#) – PLOS ONE (Feb 25)
- [Self-Reported Memory Problems Eight Months after Non-Hospitalized COVID-19 in a Large Cohort](#) – MedRxiv (Feb 26)
- [Importance of Non-Pharmaceutical Interventions in Lowering the Viral Inoculum to Reduce Susceptibility to Infection by SARS-CoV-2 and Potentially Disease Severity](#) – The Lancet Infectious Diseases (Feb 22)
- [External Validity of Phase III Trials on Vaccines against SARS-CoV-2 to a Middle-Aged and Elderly Western European Population](#) – European Journal of Epidemiology (Feb 26)
- [Covid-19: One in Seven People in England Have Antibodies from Infection or Vaccination, Finds Study](#) – BMJ (Feb 25)
- [A Neanderthal OAS1 Isoform Protects Individuals of European Ancestry against COVID-19 Susceptibility and Severity](#) – Nature Medicine (Feb 25)

*Report prepared by the UW Alliance for Pandemic Preparedness and Global Health Security and the START Center in collaboration with and on behalf of WA DOH COVID-19 Incident Management Team*