



2019-nCoV Literature Situation Report (Lit Rep)

February 3, 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

- **A randomized trial (RECOVERY) of azithromycin to treat COVID-19 found no differences between treatment and placebo groups in terms of survival, duration of hospitalization, proportion of patients discharged alive within 28 days, or proportion of patients meeting composite endpoints of mechanical ventilation or death. [More](#)**
- **Interim analysis of data from the University of Oxford studies of the ChAdOx1 (Oxford-AstraZeneca) vaccine suggested that lengthening the interval between vaccination doses was associated with increases in the clinical efficacy. The efficacy after the second dose was 82% with an interval of 12+ week between doses, compared to 55% with <6 weeks. Antibody responses were more than twice as high after a 12+ week interval between doses compared to <6 weeks among those who were 18-55 years old. Reduced viral shedding among vaccinated participants suggests a potential for reduced transmissibility. [More](#)**
- **The 501Y.V1 SARS-CoV-2 variant (first identified in the UK) had around 10 times higher binding affinity for human ACE2 than the N501-RBD strain, suggesting a potential mechanism for the observed increase in infectivity of this strain. [More](#)**

Non-Pharmaceutical Interventions

- A study conducted in South Korea of 53 children with COVID-19 found that the risk of virus transmission to their caregivers was low, with no caregivers (n=15) in the study becoming ill when they used facemasks and practiced hand hygiene in an isolation unit. COVID-19 policies in South Korea require infected individuals to be admitted to isolation units in hospitals and residential treatment centers. The study found that most children were already symptomatic by the time they entered the isolation period, and had a mild clinical course of illness, leading the authors to suggest that children with COVID-19 can be cared for at home.

Yun et al. (Feb 2021). Limited Benefit of Facility Isolation and the Rationale for Home Care in Children with Mild COVID-19. Journal of Korean Medical Science.

<https://doi.org/10.3346/jkms.2021.36.e45>

Transmission

- A cross-sectional study of US Marine Recruits (n=3,249) conducted from Spring-Fall 2020 found a baseline IgG seroprevalence against SARS-Cov-2 of 9%. Participants were primarily males aged 18-20 from the Eastern US or states with large populations. Participants who identified as Hispanic or non-Hispanic Black had higher IgG prevalence (18%, OR=3.8 and 15%, OR=3.5, respectively) than those who identified as white. Seropositivity was also greater in women than men (13% vs. 9%, OR=1.6)



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Letizia et al. (Apr 2021). SARS-CoV-2 Seropositivity among US Marine Recruits Attending Basic Training, United States, Spring–Fall 2020. *Emerging Infectious Diseases*.
<https://doi.org/10.3201/eid2704.204732>

- The risk of transmission of COVID-19 was greater when the index case had a higher concentration of virus. A cohort study of 282 COVID-19 clusters (n=314 patients) in Spain conducted from March–April 2020 indicated that the risk of symptomatic COVID-19 was associated with the viral load of the index case. The secondary attack rate ranged from 12% when the index case had a lower viral load ($< 1 \times 10^6$ copies per mL) to 24% with a higher load ($>1 \times 10^{10}$ copies per mL) (aOR=1.3 per \log_{10} increase in viral load). Increased risk of transmission was also associated with household contact with an infected person (aOR=3.0) and older age of the contact (aOR=1.02 per year). Time to onset of symptomatic COVID-19 also decreased with increased viral load, from a median of 7 days (IQR 5–10) for individuals with lower initial viral load to 5 days for those with a higher initial load.

Marks et al. (Feb 3, 2021). Transmission of COVID-19 in 282 Clusters in Catalonia, Spain: A Cohort Study. *The Lancet Infectious Diseases*.

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30985-3/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30985-3/fulltext)

Geographic Spread

- An analysis of 1,365 SARS-CoV-2 genomic sequences in South Africa identified 16 new lineages of the virus isolated between March 6 and August 26, 2020. Three lineages (B.1.1.54, B.1.1.56 and C.1) were responsible for 42% of all infections in South Africa during the first wave, during which 42 detectable lineages were circulating throughout the country. By the end of August, the C.1 lineage was the most geographically widespread, while an earlier B.1.106 (identified in April, 2020) became extinct after outbreaks were contained. The authors suggest that the rapid spread of some lineages may have been due to outbreaks rather than enhanced fitness.

Tegally et al. (Feb 2, 2021). Sixteen Novel Lineages of SARS-CoV-2 in South Africa. *Nature Medicine*. <https://doi.org/10.1038/s41591-021-01255-3>

Testing and Treatment

- A randomized open-label trial (RECOVERY) of azithromycin for COVID-19 found no significant differences in survival (rate ratio=0.97), duration of hospital stay (median 10 vs 11 days), or proportion of patients discharged from the hospital alive within 28 days (RR=1.04) between participants receiving azithromycin versus usual care. Among patients not receiving mechanical ventilation at baseline, no significant difference was observed in the proportion of patients meeting composite endpoints of mechanical ventilation or death (RR=0.95).

Abaleke et al. (Feb 3, 2021). Azithromycin in Patients Admitted to Hospital with COVID-19 (RECOVERY): A Randomised, Controlled, Open-Label, Platform Trial. *The Lancet*.

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00149-5/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00149-5/fulltext)

- A study modeling the clinical sensitivity of assays to detect SARS-CoV-2 based on their limits of detection (LoD) found that each 10-fold increase in LoD was expected to lower the assay sensitivity by about 13%. Ct values were obtained from 4,700 SARS-CoV-2 positive patients using the Abbott SARS-CoV-2 EUA test. The authors argue that assays with the highest LoD's (i.e. incapable of detecting low copy numbers) will miss a majority of infected individuals.

Arnaout et al. (Feb 3, 2020). The Limit of Detection Matters: The Case for Benchmarking Severe Acute Respiratory Syndrome Coronavirus 2 Testing. *Clinical Infectious Diseases*.

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/cia1382/6127024>

Vaccines and Immunity

- [Pre-print, not peer-reviewed] Sera from 12 participants who received either the inactivated virus vaccine BBIP-CorV or the ZF2001 RBD protein subunit vaccine (both manufactured in China) showed neutralizing activity against the 501Y.V2 SARS-CoV-2 variant (first identified in South Africa). Neutralization was measured by microcytopathogenic effect assay and there were slightly reduced geometric mean antibody titers (about 1.6-fold for each vaccine) in the sera from participants vaccinated with either vaccine compared to those against the wild type D614G strain.
Huang et al. (Feb 2, 2021). Neutralization of SARS-CoV-2 VOC 501Y.V2 by Human Antisera Elicited by Both Inactivated BBIBP-CorV and Recombinant Dimeric RBD ZF2001 Vaccines. BioRxiv. <https://doi.org/10.1101/2021.02.01.429069>
- [Pre-print, not peer-reviewed] Exploratory analysis of interim data from the University of Oxford studies of the ChAdOx1 (Oxford-AstraZeneca) vaccine suggested that lengthening the interval between vaccination doses was associated with increases in clinical efficacy. In the standard dose group (since approved by the MHRA and other international regulators), the efficacy after the second dose was 82% at 12+ weeks, compared with 55% at <6 weeks and antibody responses were more than twice as high after 12+ weeks compared to <6 weeks among those who were 18-55 years of age. Due to a mishap with calculating the concentration of study product, a subset of participants had received a lower dose (LD) of the vaccine for the first dose (approximately one half of the intended dose) which did not affect clinical efficacy. Additionally, in a subset of participants who elected not to receive the second dose, the efficacy of a sole dose of the ChAdOx1 nCoV-19 (Oxford-AstraZeneca) was 76% and protection did not decline during the 3-month period following the initial vaccination.
- Participants in the study also received weekly swabs to look for detectable nucleic acid in the absence of symptoms. Overall reduction in PCR+ samples was 54% (45%-62%), suggesting a potential for reduced transmissibility.
Voysey et al. (Feb 1, 2021). Single Dose Administration , and the Influence of the Timing of the Booster Dose on Immunogenicity and Efficacy of ChAdOx1 NCoV-19 (AZD1222) Vaccine. SSRN. <https://ssrn.com/abstract=3777268>
- [Pre-print, not peer-reviewed] Weighted analysis of results from a nationally-representative survey of US adults (n=1,592) from September 1-7, 2020 showed that 59% of the population were willing or extremely willing to take the COVID-19 vaccine as soon as it became publicly available, while almost 68% of respondents were willing or extremely willing to take the influenza vaccine. Males were significantly more willing to receive the COVID-19 vaccine than females (aOR=1.98), and participants who identified as Black were significantly less willing to take the vaccine than those who identified as white (aOR=0.59). Uncertainty about safety (37%) and efficacy (19%) were the most common concerns cited by vaccine-hesitant individuals.
Gibson et al. (Feb 2, 2021). COVID-19 Vaccine Acceptability and Inequity in the United States Results from a Nationally Representative Survey. MedRxiv. <https://doi.org/10.1101/2021.01.29.21250784>
- [Pre-print, not peer-reviewed] The receptor binding domain (RBD) of the 501Y.V1 SARS-CoV-2 variant (first identified in the UK) has around a 10-times higher binding affinity for human ACE2 than the RBD of the parent N501 strain, suggesting a potential mechanism for the higher rate of contagiousness observed with this strain. Sera collected from individuals immunized with the Pfizer-BioNTech vaccine could block the binding of Y501-RBD to ACE2, albeit to a slightly lesser degree than wild type. The therapeutic antibody bamlanivimab, however, bound the Y501-RBD as efficiently as the N501-RBD.

Clinical Characteristics and Health Care Setting

- Twenty percent of COVID-19 patients presented with GI symptoms, according to a meta-analysis. In 125 studies included in the analysis, GI symptoms upon presentation to care included loss of appetite (20%), altered sense of taste or loss of taste (15%), diarrhea (13%), nausea (10%), and vomiting of blood (9%). Over 26% of patients had confirmed positive fecal RNA, with persistent viral shedding (average 19.2 days). Patients with GI symptoms at admission to hospital had a higher risk of complications, including acute respiratory distress syndrome (RR=8.16), acute cardiac injury (RR=5.36), acute kidney injury (RR=5.52), ICU admission (RR=2.56), and mortality (RR=2.01).

Elshazli et al. (Feb 2, 2021). Gastroenterology Manifestations and COVID-19 Outcomes: A Meta-Analysis of 25,252 Cohorts among the First and Second Waves. Journal of Medical Virology. <https://onlinelibrary.wiley.com/doi/10.1002/jmv.26836>

Mental Health and Personal Impact

- Suicide rates in Japan increased among both men and women during 2020. The cross-sectional study included data from 90,048 people who died of suicide from 2016 to 2020, and based on trends from 2011-2019, the increase in suicides was most pronounced among men under age 30 (RR=1.48) and women under 30 (RR=2.14) and 30 to 49 (RR=2.30).

Sakamoto et al. (Feb 1, 2021). Assessment of Suicide in Japan During the COVID-19 Pandemic vs Previous Years. JAMA Network Open.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775740>

- A pilot randomized trial of a group Zoom intervention for loneliness among community-dwelling older adults (aged 65-90) found significant improvements in loneliness and depressive symptoms. The intervention was comprised of online guided group sessions taught by clinical social workers in which participants learned and practiced behavioral and cognitive techniques for coping with isolation due to the pandemic and the control group consisted of participants assigned to a wait list. Loneliness score (range 3-9) decreased from a mean of 5.4 to 4.8 in the intervention group and the intervention and control group differed significantly in their scores at follow-up.

Shapira et al. (Apr 2021). A Pilot Randomized Controlled Trial of a Group Intervention via Zoom to Relieve Loneliness and Depressive Symptoms among Older Persons during the COVID-19 Outbreak. Internet Interventions. <https://doi.org/10.1016/j.invent.2021.100368>

Modeling and Prediction

- As of October 2020, SARS-CoV-2 transmission in the US was estimated to be largely driven by individuals between 20-49 years of age, with at least 65 of every 100 infections originating from this age group. Using cell phone mobility data to reconstruct contact patterns, a Bayesian contact-and-infection model was used to analyze age-specific mobility trends for more than 10 million people. The model estimated that until mid-August 2020, the percent contribution to onward spread was estimated to be around 35% from individuals aged 20-34, and 41% from individuals aged 35-49. School reopenings were not found to result in substantial increases in COVID-19 attributable deaths and adults age 20-49 accounted for an estimated 72% of infections after schools reopened, compared to less than 5% originating from children aged 0-9 and less than 10% from teens aged 10-19.

Monod et al. (Feb 2, 2021). Age Groups That Sustain Resurging COVID-19 Epidemics in the United States. Science. <https://doi.org/10.1126/science.abe8372>

Other Resources and Commentaries

- [Covid-19: Surge Testing for the South Africa Variant Begins in England](#) – BMJ (Clinical Research Ed.) (Feb 2021)
- [Addressing the COVID-19 Pandemic Among Persons Experiencing Homelessness: Steps to Protect a Vulnerable Population](#) – Journal of General Internal Medicine (Feb 2 2021)
- [Rethink How We Plan Research to Shrink COVID Health Disparities](#) – Nature (Feb 4 2021)
- [Privacy Concerns Can Explain Unwillingness to Download and Use Contact Tracing Apps When COVID-19 Concerns Are High](#) – Computers in Human Behavior (Jan 2021)
- [Swallowing and Voice Outcomes in Patients Hospitalised with COVID-19: An Observational Cohort Study](#) – Archives of Physical Medicine and Rehabilitation (Jan 2021)
- [Azithromycin, RECOVERY, and the Power of Large, Simple Trials](#) – The Lancet (Feb 3 2021)
- [High Concentration and High Dose of Disinfectants and Antibiotics Used during the COVID-19 Pandemic Threaten Human Health](#) – Environmental Sciences Europe (Jan 29 2021)
- [Covid-19: People Who Have Had Infection Might Only Need One Dose of mRNA Vaccine](#) – BMJ (Feb 2 2021)
- [RAY CRISPR Diagnostic for Rapid and Accurate Detection of SARS-CoV2 Variants on a Paper Strip](#) – MedRxiv (Feb 3 2021)
- [Impact of Face Masks on 6-Minute Walk Test in Healthy Volunteers](#) – Pulmonary Circulation (Jan 20 2021)

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