

2019-nCoV Literature Situation Report (Lit Rep)

July 24, 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

- **A county-level study of the US found that nearly all counties that achieved a 70% reduction in visits to non-essential businesses brought the effective reproduction number (R_t) below 1.** [More](#)
- **Preliminary results from two different Phase 1-2 vaccine trials (UK and China) demonstrated strong humoral and cellular immune responses with no evidence of severe adverse events.**
- **Out of 120 neonates born to COVID-19 positive moms, 83% of whom roomed with their mothers and all of whom were allowed to breastfeed, none tested positive for SARS-CoV-2 or developed symptoms of COVID-19.** [More](#)
- **An extensive outbreak investigation in a school (grades 7-12) in Israel found evidence of SARS-CoV-2 transmission within the school. There was an indication that transmission was largely confined to specific grades and to individual classrooms within those grades.** [More](#)
- **A rare X-chromosome variant that impairs interferon response was identified in two pairs of brothers with severe COVID-19 despite young age (mean 26) and absence of comorbidities.** [More](#)

Non-Pharmaceutical Interventions

- Ruben et al analyzed the effect of social distancing, population density, and temperature on effective reproduction number (R_t) in 211 counties in 46 US states and the District of Columbia (total population 178,892,208). Mean peak reduction in visits to non-essential businesses in early- to mid-April was 69% and a 50% decrease in such visits was associated with a 45% decrease in R_t . A 70% reduction in such visits brought 96% of such counties below $R_t < 1$. Median case incidence and fatality rates were 10 times higher for the top decile of population density than for the lowest quartile (mean R_t in the first two weeks being 5.7 versus 3.1). Relative R_t decreased as temperatures warmed from 32°F to 52°F (0°C to 11°C), increased between 52°F and 68°F (11°C and 20°C), then again declined above 68°F (20°C).

Rubin et al. (July 2020). Association of Social Distancing, Population Density, and Temperature With the Instantaneous Reproduction Number of SARS-CoV-2 in Counties Across the United States. JAMA Network Open. <https://doi.org/10.1001/jamanetworkopen.2020.16099>

Transmission

- An extensive outbreak investigation in a school (grades 7-12) in Jerusalem (Israel) found evidence of SARS-CoV-2 transmission within the school. After re-opening on May 17 after a two month closure, the first school outbreak occurred 10 days later. There was an indication that transmission was largely confined to certain grades, and to specific classrooms within those grades.

- As part of the outbreak investigation, SARS-CoV-2 testing was conducted on 1,161 of 1,164 students and 151 of 152 staff members. Overall, 13.2% of students and 16.6% of staff had SARS-CoV-2 infection, of whom 43% of students and 76% of staff were symptomatic. One emergency room visit was recorded and there were no hospitalizations.
- Prevalence of SARS-CoV-2 among students in the school at the time of testing was highest in grades 7-9 (17.3% to 32.6%) compared to grades 10-12 (1.6%-4.5%). Even within the younger grades, cases appeared to be clustered within specific classrooms.
- An environmental school inspection reported crowded classes (35-38 students per class). While facemasks were initially required, this mandate was removed during a heatwave that occurred within days of the school re-opening.
- Contact tracing of close contacts of cases from the school identified 87 additional cases. [EDITORIAL NOTE: From this report, it is not clear how many close contacts were tested or the proportion of contacts who were positive for symptomatic versus asymptomatic cases]
 Stein-Zamir et al. (July 23, 2020). A Large COVID-19 Outbreak in a High School 10 Days after Schools' Reopening, Israel, May 2020. *Eurosurveillance*.
<https://doi.org/10.2807/1560-7917.ES.2020.25.29.2001352>
- In a cohort study of 1,481 deliveries at New York Presbyterian Hospitals in New York City between March 22 and May 17, 116 (8%) of mothers tested positive for SARS-CoV-2, corresponding to 120 neonates. All neonates were negative for SARS-CoV-2 at 24 hours of life; of the 96% that received a repeat test at 5-7 days and the 88% that were tested at 14 days, none were positive. No infants developed symptoms of COVID-19. Eighty three percent were roomed with their mothers and all were allowed to breastfeed; 78% were still breastfeeding at 5-7 days postpartum.
 Salvatore et al. (July 2020). Neonatal Management and Outcomes during the COVID-19 Pandemic: An Observation Cohort Study. *The Lancet Child & Adolescent Health*.
[https://doi.org/10.1016/S2352-4642\(20\)30235-2](https://doi.org/10.1016/S2352-4642(20)30235-2)

Testing and Treatment

- Among 436 convalescent plasma donations collected from individuals with confirmed (59%) or suspected (41%) SARS-CoV-2 infection by the UK National Health Service at least 30 days after diagnosis, 87% were positive for IgG antibodies and 76% were positive for neutralizing antibodies. Among those with confirmed SARS-CoV-2, 99% had IgG antibodies and 88% had neutralizing antibodies. Neutralizing antibody titers were high enough to be used for treatment of other SARS-CoV-2 patients in 34% of donations, with the higher levels associated with confirmed infection, prior hospitalization, older age, and more recent diagnosis. Antibody levels declined over three months following diagnosis.
 Harvala et al. (July 2020). Convalescent Plasma Treatment for SARS-CoV-2 Infection: Analysis of the First 436 Donors in England, 22 April to 12 May 2020. *Euro Surveillance*.
<https://doi.org/10.2807/1560-7917.ES.2020.25.28.2001260>
- [pre-print, not peer-reviewed] O'Keefe et al. describe the use of a risk assessment tool for telemedicine assessment of outpatients diagnosed with COVID-19. Out of 496 patients with COVID-19 confirmed by self-testing, increasing risk tier was positively associated with risk of hospitalization (Tier 2 vs Tier 1: HR=3.74; Tier 3 vs Tier 1: HR=10.87) (adjusted for age, gender, and obesity).
 O'Keefe et al. (July 24, 2020). Initial Experience in Predicting the Risk of Hospitalization of 496 Outpatients with COVID-19 Using a Telemedicine Risk Assessment Tool. Pre-print downloaded July 24 from <https://doi.org/10.1101/2020.07.21.20159384>

- A systematic literature review (37 studies, 22 used in meta-analysis) showed consistent recovery of SARS-CoV-2 genetic material from the upper respiratory tract (URT), the lower respiratory tract (LRT), and the feces, regardless of clinical severity. SARS-CoV-2 was found to persist for longer in moderate-to-severe patients versus mild patients for both the URT and feces, and to persist for longer in the LRT than URT in adult patients. Viral load was also found to peak in earlier stages of infection in the URT compared to the LRT.

Weiss et al. (Aug 1, 2020). Spatial and Temporal Dynamics of SARS-CoV-2 in COVID-19 Patients: A Systematic Review and Meta-Analysis. EBioMedicine.

<https://doi.org/10.1016/j.ebiom.2020.102916>

Vaccines

- Folegatti present preliminary results of a phase 1/2 single-blind, randomized multi-center (5 UK sites) trial of a chimpanzee adenovirus-vectored vaccine expressing the SARS-CoV-2 spike protein (n=543 treatment and n=534). Controls received a meningococcal conjugate vaccine. Adverse effects were more common in the treatment arm and included pain, fever, chills, muscle ache, and malaise. No serious adverse events were reported. Cell-mediated immunity peaked on day 14, and humoral (antibody) response rose by day 28 and was boosted by following a second dose in 10 participants assigned (non-randomly) to an unblinded boost group. Neutralizing antibody response was detected in all participants and was strongly associated with antibody levels.

Folegatti et al. (July 2020). Safety and Immunogenicity of the ChAdOx1 NCoV-19 Vaccine against SARS-CoV-2: A Preliminary Report of a Phase 1/2, Single-Blind, Randomised Controlled Trial. The Lancet. [https://doi.org/10.1016/S0140-6736\(20\)31604-4](https://doi.org/10.1016/S0140-6736(20)31604-4)

- Zhu et al. report findings from a phase 2 randomized, double-blind, placebo-controlled single-center (Wuhan) trial of an Ad5-vectored COVID-19 vaccine. A total of 508 participants were randomly assigned to treatment (n=253 low dose, n=129 medium dose) or placebo (n=126; vaccine excipients with no viral particles). Both treatment groups had high seroconversion rates by 28 days (96% in the low dose group and 97% in the high dose group) and demonstrated significant neutralizing antibody responses, as well as significant T-cell responses. Adverse reactions were reported in 72% and 74% of the low- and high-dose treatment arms, versus 9% of the placebo arm, all of which were self-limiting and resolved within 72-96 hours without medication. No serious adverse reactions were documented within 28 days.

Zhu et al. (July 2020). Immunogenicity and Safety of a Recombinant Adenovirus Type-5-Vectored COVID-19 Vaccine in Healthy Adults Aged 18 Years or Older: A Randomised, Double-Blind, Placebo-Controlled, Phase 2 Trial. The Lancet. [https://doi.org/10.1016/S0140-6736\(20\)31605-6](https://doi.org/10.1016/S0140-6736(20)31605-6)

Clinical Characteristics and Health Care Setting

- A rare genetic mutation was identified in two sets of brothers who had severe COVID-19 disease. A case series reported by van der Made et al. included two sets of brothers under age 35 (mean age 26) without pre-existing medical conditions who were hospitalized with severe COVID-19 in the Netherlands. All four men required mechanical ventilation in the ICU and one died. Whole-exome sequencing and basic genetic and immunological tests identified a loss-of-function X-chromosomal *TLR7* gene variant that is associated with impaired type I and II interferon responses.

van der Made et al. (2020). Presence of Genetic Variants Among Young Men With Severe COVID-19. JAMA. <https://doi.org/10.1001/jama.2020.13719>

- A telephone survey of non-hospitalized symptomatic COVID-19 patients found that illness can be prolonged, even among young adults without underlying chronic medical conditions. Among 274 symptomatic COVID-19 patients interviewed 14-21 days after diagnosis, 65% percent had returned to their usual state of health a median of 7 days (IQR 5-12 days) after testing, while the 35% had not yet returned to their usual state of health. Older age and presence of chronic medical conditions were associated with a higher risk of not having returned to normal health. Among those with no chronic medical conditions and in the youngest age group (18-34 years), 19% had not returned to normal health by 14-21 days after diagnosis.

Tenforde et al. (July 24, 2020). Symptom Duration and Risk Factors for Delayed Return to Usual Health Among Outpatients with COVID-19 in a Multistate Health Care Systems Network — United States, March–June 2020. MMWR. <https://doi.org/10.15585/mmwr.mm6930e1>

Mental Health and Personal Impact

- An analysis of longitudinally collected social network parameters and mental health outcomes among two cohorts (n=212 and n=57) of Swiss undergraduate students before and during the COVID-19 pandemic found that social networks were sparser during the pandemic and students were more likely to study in isolation; however friendship and social support networks did not differ significantly between the two periods. Stronger social ties were more likely to be maintained but there was an increasing number of isolated individuals. Students were on average more depressed, slightly more anxious, more stressed, and felt more lonely during the pandemic compared to half a year earlier. Some students reported that the crisis situation affected their lives positively by reducing “Fear of Missing Out” and competition among the students.

Elmer et al. (2020). Students under Lockdown: Comparisons of Students’ Social Networks and Mental Health before and during the COVID-19 Crisis in Switzerland. PloS One. <https://doi.org/10.1371/journal.pone.0236337>

Modeling and Prediction

- *[pre-print, not peer-reviewed]* Using a transmission dynamic model calibrated to US state-level COVID-19 cases and deaths from March to June, Chiu et al. found that most states were able to achieve $R_1 < 1$ through stay-at-home orders. However by June 20, only 19 states and the District of Columbia were on track to control COVID-19 at current levels of re-opening, 24 or the remaining 31 states needed to double their current testing and/or contact tracing to control COVID-19, and 7 of these 24 also needed to restrict social contact by another 25%.

Chiu et al. (July 2020). State-Level Impact of Social Distancing and Testing on COVID-19 in the United States. Pre-print downloaded July 24 from <https://doi.org/10.21203/rs.3.rs-40364/v1>

Public Health Policy and Practice

- Signorelli et al. analyze COVID-19 mortality rates and case fatality in 9 high-income metropolitan regions in Europe and the US with similar socio-demographic characteristics, daytime commuting populations, and business activities. While the crude mortality rate was highest for the Lombardy Region in Italy, after age-standardization New York State had the highest mortality rate.

Signorelli et al. (July 2020). COVID-19 Mortality Rate in Nine High-Income Metropolitan Regions. Acta Bio-Medica. <https://doi.org/10.23750/abm.v9i19-S.10134>

Other Resources and Commentaries

- [Why COVID-19 Models Should Incorporate the Network of Social Interactions](#) – Physical Biology (July 23)
- [Model-Free Estimation of COVID-19 Transmission Dynamics from a Complete Outbreak](#) – Medrxiv (July 24)
- [Reducing COVID-19 Hospitalization Risk through Behavior Change](#) – Medrxiv (July 24)
- [COVID-19-like Symptoms Observed in the Chinese Tree Shrews Infected with SARS-CoV-2](#) – Zoological Research (July 23)
- [COVID-19 and Living Space Challenge. Well-Being and Public Health Recommendations for a Healthy, Safe, and Sustainable Housing](#) – Acta Bio-Medica : Atenei Parmensis (July 20)
- [Protecting Higher Education Institutions from COVID-19: Insights from an Italian Experience](#) – Journal of American College Health : J of ACH (July 23)
- [Distancing Without Isolating](#)—Connection in the Era of COVID-19 – JAMA Oncology (July 23)
- [From People to Panthera Natural SARS-CoV-2 Infection in Tigers and Lions at the Bronx Zoo](#) – Biorxiv (July 23)
- [Surveillance for Probable COVID-19 Using Structured Data in the Electronic Medical Record](#) – Infection Control and Hospital Epidemiology (July)
- [No Body Is Expendable: Medical Rationing and Disability Justice during the COVID-19 Pandemic](#) – The American Psychologist (July)
- [We Are at Risk Too The Disparate Impacts of the Pandemic on Younger Generations](#) – Medrxiv (July 24)
- [COVID-19: From a PHEIC to a Public Mental Health Crisis?](#) – The Lancet Public Health (July 23)
- [Pharmacotherapy in COVID-19 Patients: A Review of ACE2-Raising Drugs and Their Clinical Safety](#) – Journal of Drug Targeting (July 23)
- [The Role of Public Health in COVID-19 Emergency Response Efforts From a Rural Health Perspective](#) – Preventing Chronic Disease (July 23)

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