JULY 23, 2020

The scientific literature on COVID-19 is rapidly evolving and these articles were selected for review based on their relevance to 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.

The COVID-19 Literature Report is researched, compiled, and edited daily by students and faculty in the University of Washington Schools of Public Health and Medicine. The editors are Brandon Guthrie PhD and Jennifer Ross MD MPH. Contributors include Diana Tordoff MPH, Julianne Meisner BVM&S MS, Lorenzo Tolentino BS, Wenwen Jiang MPH, Sherrilynne Fuller PhD FACMI, Dylan Green MPH, Diana Louden MLib, Ashley Tseng MPH and Jessie Seiler MPH.

Today's summary is based on a review of 264 articles (244 published, 20 in preprint).

KEY TAKEAWAYS

- Residents in long-term care facilities in Ontario, Canada had a 13-fold higher risk of death from COVID-19 compared to community-living adults age 70 and older. More
- Across 9 countries, age-standardized COVID-19 case fatality was 1.9%. There was wide variation in unadjusted country-level case-fatality, ranging from 0.7% in Germany to 9.3% in Italy. Adjustment for the age distribution of cases explained 66% of the between-country variation. More
- Compared to clinician-collected nasopharyngeal swabs, unsupervised self-collected midnasal swabs had a sensitivity of 80.0% and a specificity of 97.9% for diagnosing SARS-CoV-2. More
Non-Pharmaceutical Interventions

- Callow et al. gauged opinion and behaviors regarding COVID-19 and the Maryland Governor’s lifting of lockdown restrictions among a convenience sample of 242 older adults. They found that attitudes toward social isolation were affected by perceived benefits and barriers to social distancing measures, perceived severity of COVID-19, and political affiliation.


Transmission

- Intergenerational relationships (e.g., cohabitation and contact between family members of different generations) have been hypothesized to play a role in COVID-19 spread and case fatality. Using data from 19 European counties, Arpino et al. found that at the country level, higher levels of intergenerational relationships are associated with higher COVID-19 case fatality, although the magnitude of the association is small. At the subnational level, an opposite association is often observed. The authors advocate for policies that take into consideration the important instrumental and emotional support that intergenerational ties provide, which may increase compliance to the lockdown and "phase-2" restrictions.

  Arpino et al. (July 22, 2020). No Clear Association Emerges between Intergenerational Relationships and COVID-19 Fatality Rates from Macro-Level Analyses. PNAS. https://doi.org/10.1073/pnas.2008581117

- Korber et al. present evidence that SARS-CoV-2 viruses with the G614 mutation in the Spike protein are more prevalent than the original D614 form identified in the first human cases in Wuhan, China. In a follow-up study of 999 COVID-19 patients at the Sheffield Teaching Hospitals, patients infected with G614 shed more viral nucleic acid compared with those with D614 (p=0.037), and G614-viruses show significantly higher
infectious titers in vitro than their D614 counterparts (2.6- to 9.3-fold increase, p<0.0001).

[https://doi.org/10.1016/j.cell.2020.06.043](https://doi.org/10.1016/j.cell.2020.06.043)

## Testing and Treatment

- Compared to clinician-collected swabs, home-based self-collected swabs had a sensitivity of 80.0% (95% CI: 63-91%) and a specificity of 97.9% (95% CI: 94-99.5%). These results were based on a cohort of 185 symptomatic people who presented at drive-through clinics in Washington State who underwent both an unsupervised home self-collected swab and a clinician-collected nasopharyngeal swabs for diagnosis of SARS-CoV-2 infection by RT-PCR.


- A review of 9 studies (293 total samples) found no statistically significant difference in viral loads between saliva, nasopharyngeal, or sputum specimens obtained for the detection of SARS-CoV-2. The authors suggest that these findings indicate that self-collected saliva may be a reliable and non-invasive approach for the detection of SARS-CoV-2 using RT-PCR.

[https://doi.org/10.1186/s40249-020-00728-w](https://doi.org/10.1186/s40249-020-00728-w)

- TMPRSS2 is a cellular protease gene that activates SARS-CoV-2 for entry into lung cells. Hoffmann et al. report that the engineered expression of TMPRSS2 in ex-vivo Vero cells renders SARS-CoV-2 infection insensitive to chloroquine. Moreover, chloroquine did not block SARS-CoV-2 infection in TMPRSS2-positive lung cells. The authors conclude results indicate that chloroquine targets a pathway for viral activation that is not operative in lung cells and is unlikely to protect against SARS-CoV-2 spread in and between patients.

  Hoffmann et al. (July 22, 2020). Chloroquine Does Not Inhibit Infection of Human Lung Cells
• Ramiro et al. evaluated clinical records of 86 patients with severe COVID-19-associated cytokine storm syndrome who received an intensive course of glucocorticoids. Compared to an untreated historical group of patients who received supportive care only (1:1 match on sex and age), treated patients had a higher rate of reaching respiratory recovery (HR=1.8), were less likely to die (HR=0.35), and had a lower rate of invasive mechanical ventilation (HR=0.29).

Ramiro et al. (July 20, 2020). Historically Controlled Comparison of Glucocorticoids with or without Tocilizumab versus Supportive Care Only in Patients with COVID-19-Associated Cytokine Storm Syndrome: Results of the CHIC Study. Annals of the Rheumatic Diseases. https://doi.org/10.1136/annrheumdis-2020-218479

Clinical Characteristics and Health Care Setting

• Based on a cohort study among 627 long-term care (LTC) facilities in Ontario, Canada, the incidence of deaths related to COVID-19 was 13-fold higher among LTC residents compared to adults older than 69 years living in the community. This excess risk increased from 8-fold to 87-fold between March 29 and April 11. Infection among LTC staff was associated with death among residents with a 6-day lag.


• In a cross-sectional study using population-based data on COVID-19 cases and deaths in 9 countries, Sudharsanan et al. observed an overall large variation in case-fatality. The highest case-fatality was reported in Italy (9.3%), and the lowest in Germany (0.7%). Adjustment for the age distribution of cases explains 66% of the between-country variation. The resulting age-standardized median case fatality was 1.9%. The authors conclude that it is important to focus on age-adjusted case fatality when comparing performance in caring for patients with COVID-19 and for monitoring the epidemic over time.

Sudharsanan et al. (July 22, 2020). The Contribution of the Age Distribution of Cases to COVID-19 Case Fatality Across Countries: A 9-Country Demographic Study. Annals of Internal
Based on data from the 2018 Behavioral Risk Factor Surveillance System (BRFSS) survey, the median county prevalence of any of five underlying medical conditions (chronic obstructive pulmonary disease, heart disease, diabetes, chronic kidney disease, and obesity) that are associated with increased risk for severe COVID-19 disease was 47% across 3,142 U.S. counties. While the total number of those with co-morbidities follows the overall population distribution, the prevalence of co-morbidities is higher in the southeastern United States and in more rural counties. County-level maps are provided to support local decision-makers in identifying areas at higher risk for severe COVID-19 illness.


Modeling and Prediction

[Preprint, not peer reviewed] Steyn et al. predicted the risk of undetected COVID-19 cases within managed isolation and quarantine facilities and the risk of infectious cases being released into the community using data during a two-week period (June 23 to July 6, 2020) in New Zealand.

• Under the current 14-day quarantine order, a combination of testing on days 3 and 12, daily symptom checks, and complete isolation of confirmed cases would reduce the risk of releasing an infectious case to an estimated 0.1% per arriving case. Shorter quarantine periods or reliance on testing only with no quarantine substantially increased the predicted risk. The ratio of cases detected on day 3 versus day 12 could be an effective indicator of the level of transmission.

Steyn et al. (July 22, 2020). The Effect of Border Controls on the Risk of COVID-19 Reincursion from International Arrivals. Pre-print downloaded July 23 from https://doi.org/10.1101/2020.07.15.20154955

Adekunle et al. estimated that there was a 79% reduction in imported COVID-19 cases in Australia as of March 2, 2020 and a one-month delay in the COVID-19 outbreak that was attributable to the travel bans imposed on January 24, 2020. Their model results aligned with the observed imported cases in Australia.

Public Health Policy and Practice

• A large number of monoclonal antibodies that potently neutralize the SARS-CoV-2 virus were identified from COVID-19 cases from New York. Liu et al. report the isolation of 61 SARS-CoV-2-neutralizing monoclonal antibodies from 5 infected patients hospitalized with severe disease at the Columbia University Irving Medical Center in New York City. Among these are 19 antibodies that potently neutralized the authentic SARS-CoV-2 virus in vitro, 9 of which exhibited exquisite potency. Epitope mapping show these antibodies are directed to the top of the viral spike, which the authors say indicates immunogenicity. Several of these monoclonal antibodies are promising candidates for clinical development as potential therapeutic and/or prophylactic agents against SARS-CoV-2.


• [Preprint, not peer reviewed] The receptor-binding domain of the CoV spike (RBD-S) protein is important in host cell recognition and infection, and antibodies targeting this domain are often neutralizing. Graham et al. tested anti-RBD-S responses among 32 COVID-19 patients. They found that IgG, IgM, and IgA responses were all induced within 10 days following symptom onset, and IgG response was sustained over a 5-week period. No differences in responses were observed by age or sex, indicating that age-and sex-related disparities in COVID-19 fatality are not explained by anti-RBD-S responses. The authors concluded that the multi-isotype anti-RBD-S response could serve as a potential marker by which to monitor vaccine-induced responses.

Graham et al. (July 22, 2020). Kinetics and Isotype Assessment of Antibodies Targeting the Spike Protein Receptor Binding Domain of SARS-CoV-2 In COVID-19 Patients as a Function of Age and Biological Sex. Pre-print downloaded July 23 from [https://doi.org/10.1101/2020.07.15.20154443]

Public Health Policy and Practice

• A group of experts from the Spanish Association of Sexuality and Mental Health released consensus recommendations to maintain lower-risk sexual activity during the
COVID-19 pandemic. Specific recommendations include returning to engaging in safe sex for those with a stable partner after quarantine is over (28 to 33 days depending age) and if all parties are asymptomatic. Abstinence is recommended for those under quarantine, those with some clinical symptoms, health professionals in contact with COVID-19 patients, and during pregnancy. For persons without a partner, it is strongly recommended to not initiate sexual activity with a sporadic partner.


OTHER RESOURCES AND COMMENTARIES

- Are We Responsible for the Racial Inequalities of Covid-19? – BMJ (July 22)
- Covid-19 and Health Equity — Time to Think Big – New England Journal of Medicine (July 22)
- Serosurveillance and the COVID-19 Epidemic in the US – JAMA (July 21)
- A Simple Correction for Covid-19 Testing Bias – ArXiv (July 15)
- Opinion: It’s Ethical to Test Promising Coronavirus Vaccines against Less-Promising Ones – PNAS (July 22)
- Age Is Just a Number: A Critically Important Number for COVID-19 Case Fatality – Annals of Internal Medicine (July 22)
- Planning for the Post-COVID Syndrome: How Payers Can Mitigate Long-Term Complications of the Pandemic – Journal of General Internal Medicine (July 22)
- COVID-19 and Persons with Substance Use Disorders: Inequities and Mitigation Strategies – Substance Abuse (July 22)
- ADHD as a Risk Factor for Infection With Covid-19 – Journal of Attention Disorders (July 22)
- Transmission Route and Introduction of Pandemic SARS-CoV-2 between China, Italy and Spain – Journal of Medical Virology (July 22)
- On the Efficacy of Online Drug Surveys during the Time of COVID-19 – Substance Abuse (July 22)
- Pooling Data From Individual Clinical Trials in the COVID-19 Era – JAMA (July 22)
- Universal Screening for the SARS-CoV-2 Virus on Hospital Admission in an Area with Low COVID-19 Prevalence – Infection Control & Hospital Epidemiology (July 23)
- Financial Toxicity After Hospitalization; Considerations in Coronavirus Disease 2019 Recovery – Critical Care Medicine (Aug 17)
Current Medical Research and Opinion (July 22)

- The Need to Balance Basic and Clinical Research with the Safety of the Research Environment and Personnel in the Time of COVID-19 in the United States – Current Medical Research and Opinion (July 22)


The COVID-19 Lit Rep is currently prepared by the UW MetaCenter for Pandemic Preparedness and Global Health Security and the START Center in collaboration with and on behalf of the Washington State Department of Health. The Lit Rep was originally developed and disseminated by the WA DOH COVID-19 Incident Management Team to support evidence-based decision making throughout the region.