COVID-19 Research Watch
October 26, 2020

PHARMACEUTICAL INTERVENTIONS

Repurposed antiviral drugs for COVID-19 — interim WHO SOLIDARITY trial results
This study evaluated four repurposed antiviral drugs (remdesivir, hydroxychloroquine, lopinavir, and interferon-β1a) for their impact on mortality, ventilation, and length of hospital stay among those hospitalized with COVID-19. A total of 11,266 COVID-19 patients in 405 hospitals across 30 countries were randomized to receive one of the four antiretroviral medications or local standard of care without study drug. The study found that among hospitalized patients, none of these four drugs had a significant impact on mortality, ventilator requirement, or length of stay in the hospital.

This study aimed to investigate the efficacy of therapeutic agent remdesivir among adult patients hospitalized with laboratory-confirmed COVID-19 and evidence of lower respiratory tract infection. The researchers conducted a double-blind, randomized, placebo-controlled trial at 60 trial sites and 13 subsites. Of the 1114 patients who were eligible for the study, 1062 were assigned randomly to either receive placebo (521 patients) or remdesivir (541 patients) in a 1:1 ratio. A 200-mg loading dose of remdesivir was administered intravenously on day 1 followed by 100-mg maintenance dose administered daily on days 2-10 or until patients were discharged or deceased. The placebo was administered with the same schedule and volume as the patients receiving remdesivir in parallel. The mean age of patients was 58.9 years and the majority were male (64.4%). Patients who were administered remdesivir had a median recovery time of 10 days compared to patients who received the placebo whose median recovery time was 15 days. Modeling estimated that patients who received remdesivir were more likely to have a clinical improvement at day 15 (odds ratio 1.5; 95% CI, 1.2 to 1.9, after adjustment for actual disease severity) compared to patients who received placebo. The estimated mortalities found using the Kaplan–Meier were 6.7% with remdesivir and 11.9% with placebo by day 15 and 11.4% with remdesivir and 15.2% with placebo by day 29. The researchers conclude that remdesivir may have prevented the progression of more severe respiratory disease and was superior in shortening the time to recovery in adult patients who were hospitalized with COVID-19 and had evidence of lower respiratory tract infection.

PATHOPHYSIOLOGY

Comparative host-coronavirus protein interaction networks reveal pan-viral disease mechanisms
The authors of this study evaluated the SARS-CoV-2, SARS-CoV-1, and MERS-CoV viruses for shared and individual target proteins and cellular processes for the viruses. The goal of this research is to identify possible antiviral medications that will target these viruses specifically. One identified protein interaction, Tom70, which binds to the Orf9b, was shown
to be preserved between SARS-CoV-1 and SARS-CoV-2, and thus may merit further investigation for possible therapeutics. The authors also found that those who had higher sIL17RA plasma levels were less likely to develop COVID-19. Lastly, evaluation of patient medical records revealed that inpatients who were prescribed sigma-ligand typical antipsychotics - compared to atypical antipsychotics - had better outcomes related to COVID-19, possibly due to the sigma-1 receptor interaction.

**Associations between genetically predicted protein levels and COVID-19 severity**

This study aimed to identify associations between genetically predicted protein levels and COVID-19 disease severity using a predominantly European genome-wide association study platform. Of the 1357 proteins included in this study, 18 proteins were associated with severe disease. Among those with severe disease, 12 proteins remained associated with COVID-19 severity after the Bonferroni correction. Positive associations were found among six proteins (DC-SIGN, BGAT, B3GN2, C1GLC, SCF, and FA20B) with odds ratios of 1.09 to 1.66. Inverse associations of lower predicted protein level and higher levels of COVID-19 severity were identified for 12 proteins with odds ratios of 0.49 to 0.88. The findings of this study highlight a potential relationship between genetic variation in protein levels and COVID-19 severity. The identified proteins may have implications for targeting drug repurposing efforts.

**Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study**

Using a database of COVID-19 patients across 1205 practices in England, this study developed a risk prediction algorithm, QCOVID, to assess the primary outcome of time to death from COVID-19 and the secondary outcome of hospital admission. The QCOVID algorithm was first developed in a derivation cohort and then calibrated in two validation time periods. The derivation cohort consisted of approximately six million patients, of which 0.18% were hospitalized due to COVID-19 and 0.07% died due to COVID-19 within 97 days of hospital admission. The QCOVID model was able to account for 73.1% of the variation in time to death from COVID-19 among men, and similar results were found among women. The model was accurate in predicting 75.7% of deaths in patients with the highest 5% of predicted risk. In the top 20% and 25% of patients with highest predicted risk of death, the QCOVID model had a sensitivity of 94% and 96%, respectively. The results of this study indicate the usefulness of the QCOVID algorithm, with the caveat that there is a need to recalibrate and update the algorithm as the pandemic evolves.

**NON-CLINICAL TRENDS**

**Characteristics associated with racial/ethnic disparities in COVID-19 outcomes in an academic health care system**

Tian et al. conducted a retrospective study of patients who were tested and/or diagnosed with COVID-19 in the University of Michigan Health System between March 10 and April 22, 2020. Among the 5698 patients included in the cohort, 1139 (20%) tested positive for COVID-19. 3470 (65.5) of the patients were white and 1058 (18.6%) were black. This cohort was compared to a control group of 7168 untested patients from the health system.
database. Higher positive test rates were found in black patients (41.8%) than white patients (13.2%). Black patients had higher odds of getting tested and were more likely to be hospitalized (OR=1.72). Among seven different comorbidities (respiratory disease, circulatory disease, type 2 diabetes, kidney disease, liver disease, and an autoimmune disease), type 2 diabetes and kidney disease were found to have the highest hospitalization risk. White patients had a higher comorbidity burden with hospitalization and ICU admission. Additionally, white patients demonstrated an association between type 2 diabetes and hospitalizations, which was not seen among black patients. Patients living in areas of higher population density had a higher chance of hospitalization, regardless of race. Overall, there were no significant differences between race and COVID-19 outcomes, which points to structural factors being responsible for the differential outcomes.

**Covid-19, unemployment, and health: time for deeper solutions?**

Hensher describes the potential negative effects of unemployment due to the COVID-19 pandemic. Unemployment has been associated with increased all-cause mortality and increased mental distress, substance abuse, depression, and anxiety. Two primary solutions have been discussed: a job guarantee and universal basic income. A job guarantee is a federally funded standing offer for work at a livable wage with benefits such as healthcare coverage. Job guarantees act to reduce poverty and break down racial inequalities in wealth. They have demonstrated success in Argentina, South Africa, India, and many other countries. Universal basic income involves a universal and unconditional cash transfer to reduce income inequality and provide a baseline standard of living. Proponents argue for its ability to improve health and reduce health inequities through direct action on various social determinants of health. Successful universal basic income schemes have been run in countries such as Finland. Those receiving universal basic income had better employment outcomes, health, and wellbeing than those who did not. Hensher then discusses that a job guarantee better reduces poverty and inequality by ensuring everyone who wants to work has the option. In doing so, greater power is given to workers by ensuring a greater share of income flows towards labor. If unemployment is indeed the root issue of these health concerns, then a job guarantee would address this issue and should be implemented in the immediate aftermath of COVID-19.

**Findings From a Probability-Based Survey of United States Households About Prevention Measures Based on Race, Ethnicity, and Age in Response to Severe Acute Respiratory Syndrome Coronavirus**

Sauceda et al. investigated individual behaviors taken to prevent SARS-CoV-2 infection based on race, ethnicity, and age. A total of 2,029 participants were included in the sample and data were collected from April 20-26, 2020. No differences in individual behavior were observed between different racial group, except that Latinos were less likely than whites to report keeping physical distance with people outside of their households (OR: 0.49, 95% CI: 0.28-0.86). Females were more likely to engage in prevention measures than males. No differences were observed based on age. The survey also assessed the efficacy of technology-based strategies. Compared to whites, African Americans and Latinos were less likely to install an app that asks about symptoms (OR: 0.52, 95% CI: 0.38-0.70 and OR: 0.53, 95% CI: 0.40-0.70, respectively). African Americans and Latinos were less likely to use a website to log symptoms and get recommendations for COVID-19 (OR: 0.47, 95% CI:
0.33-0.65 and OR: 0.54, 95% CI: 0.40-0.71, respectively). These findings suggest that individual behavior is unlikely to account for the disproportionate impact of COVID-19 across racial and ethnic groups. Instead, it is likely that other social and structural drivers of health disparities such as racism are causing the disparities. Similarly, technology-based strategies are ineffective if they do not account for potential medical mistrust, lack of familiarity with technology, and privacy concerns.

**REGIONAL SPECIFIC LESSONS LEARNED**

**Magnitude, demographics and dynamics of the effect of the first wave of the COVID-19 pandemic on all-cause mortality in 21 industrialized countries**

Vasilis et al. used 16 Bayesian models to develop a probabilistic model averaging to understand the weekly mortality effects of COVID-19 across 21 different countries in Europe, Australia and New Zealand. Their study method provided a robust way to estimate the number of deaths that would have occurred in a non-pandemic time. Between mid-February to the end of May, there were about 206,000 deaths attributed to COVID-19, which is similar to the number of deaths caused by lung cancer in one year. Data collected from each country were broken down into four groups based on the relative number of deaths in each country. The countries with the largest death toll included Belgium, England and Wales, Scotland, Italy and Spain. The authors state the number of deaths were affected by three factors: characteristics of the population, policy and public health response, and the preparation and resilience of the public health infrastructure. This implies that policies can be put in place in the future to have a better preparedness and public health response.

**COVID-19 in New Zealand and the impact of the national response: a descriptive epidemiologic study**

Jefferies et al investigated the impact of national suppression strategies during the first wave of COVID-19 in New Zealand on all confirmed and probable cases of COVID-19 between February 2, 2020 and May 13, 2020. New Zealand’s response can be broken down into five phases. Phase 1 was the initial period of travel restrictions. Phase 2 included rapid escalation of non-pharmaceutical interventions such as 14-day self-isolation of international arrivals and bans on public gatherings. Phase 3 was the first half of lockdown that included stay-at-home orders and introduced contact tracing. Phase 4 was the second half of lockdown and was characterized by increased testing. Phase 5 was the start of easing movement restrictions. National disease databases and test result repositories were primary sources of disease data. A total of 1,503 cases were detected between February 12 and May 10, 2020. Of these, 1,153 (77%) were confirmed through laboratory testing and 350 (23%) are probable cases. The case infection rate per million people per day peaked during phase 2 at 8.5. However, within two weeks of lockdown, the daily case infection rate decreased by 62% to 3.2 and the primary source of infection was overseas. Locally acquired disease was uncommon but tended to disproportionately affect vulnerable populations and was associated with more severe outcomes. The researchers concluded that the unprecedented speed and intensity of the national response was key to New Zealand’s success. New Zealand achieved the highest score in Government Response Stringency Index, reflecting the fastest trajectory to reaching the highest alert level. The
authors attribute the country’s success to critical decisive governance, effective communication, and high population compliance.

**CLINICAL PRESENTATION AND MANAGEMENT**

*Genomic evidence for reinfection with SARS-CoV-2: a case study*¹¹

Tillett et al. described a case report of a 25-year-old male resident of Washoe County, Nevada, who was infected twice with SARS-CoV-2. The patient had no history of significant underlying conditions and no signs of compromised immunity. The patient, who had started experiencing symptoms on March 25, 2020, tested positive for SARS-CoV-2 infection with an RT-PCR test conducted on a nasopharyngeal swab on April 18, 2020 (specimen A). The patient’s symptoms disappeared on April 27 but reappeared on May 28. Another nasopharyngeal swab was collected on June 5 and tested positive for SARS-CoV-2 (specimen B). The patient reported increased symptom severity during the second infection. Specimens A and B genetically differ greatly enough to suggest that this individual is the first in North America with symptomatic reinfection with SARS-CoV-2. The researchers emphasize that the absence of comprehensive genomic sequencing of positive cases in the USA and worldwide reduces the ability to advance disease surveillance systems. Without this, it is difficult to verify the existence of reinfection and to calculate its frequency.

**TRANSMISSION PATTERNS**

*Estimating total excess mortality during a COVID-19 outbreak in Stockholm, Sweden*¹²

This study aimed to investigate how the total excess mortality developed during the COVID-19 outbreak in Stockholm, Sweden in relation to the recognized number of COVID-19-related deaths. 2020 mortality data was retrieved from the Swedish National Board of Health and Welfare, and mortality estimates for the past 10 years came from EuroStat. The mortality was calculated for the Stockholm region using the annual adjusted population statistics for Stockholm during the last 10 years. Reported COVID-19 related mortality was determined using publicly available repositories and classified by the death certificate as a COVID-19-related death. Results showed total mortality in Stockholm at the beginning of 2020 was slightly lower than the 10-year average mortality for this region; however, a rapid increase in mortality was seen at the onset of the outbreak during week 12. When comparing the number of reported COVID-19 related deaths in weeks 12-17--the peak period of the outbreak--25.6% of excess mortality during the COVID-19 epidemic were not recognized as related to COVID-19 by the data. The public health data reporting COVID-19-related deaths accounted for 74.4% of the accumulated excess mortality in Stockholm from week 12-17. The researchers suggest that total excess mortality during the COVID-19 outbreak could give a more comprehensive idea of the total burden of excess deaths from COVID-19 than what has been reported as COVID-19-related deaths and could facilitate managing future outbreaks.

**ADDITIONAL RESOURCES**

UCSF Library COVID-19 Research and Information Resources
UCSF Institute for Global Health Sciences COVID-19 Resources
Note on this Document: This document was assembled by graduate and doctoral students attending the University of California, San Francisco with the intent of facilitating the rapid dissemination of information to the global community in order to help during this time. Alyssa Becasio, Canice Christian, Diana Etwaru, James Feng, and Micaela Reyna contributed to these summaries. This work is volunteer based.

References: