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BRIEF19

A daily review of covid-19 research and policy

RESEARCH BRIEFING

Repurposed antiviral drugs unable to lower covid-19 mortality, interim WHO study finds.

A major preprint [publication](#) by scientists working with the World Health Organization (WHO) went live late last week. The “Solidarity” study is a randomized clinical trial aiming to answer a simple but important question: are patients who are hospitalized with covid-19 who receive antiviral medications less likely to die while in the hospital compared to those who receive placebo in addition to other standard care?

The Solidarity trial is a large, multi-country, open-label (not blinded) randomized study. This clinical trial, a monumental effort, has been rolled out in 405 hospitals across 30 countries with 11,266 patients randomized to one of handful of treatment arms, which included: remdesivir, hydroxychloroquine (HCQ), lopinavir, lopinavir plus interferon, interferon only, or placebo. All patients received standard of care, which was supportive treatment.

The results were sobering. 28-day mortality was 12 percent overall, and 39 percent of the patients required mechanical ventilation at the time of enrollment into the trial. The *overall* death rate ratios (RR) were as follows (note: any RR above 1 implies an increased chance of dying, any RR below 1, implies a decreased chance of dying, and 95 percent confidence intervals (CI) describe the range that the statistics are 95 percent likely to fall under; any 95% CI that “crosses” 1.0 is considered to have had no effect in either direction):

Remdesivir RR = 0.95 (95% CI, 0.81-1.11, p = 0.5); HCQ RR = 1.2 (95% CI, 0.8-1.8, p = 0.23); Lopinavir RR = 1.0 (0.8-1.3, p = 0.97); Interferon RR = 1.2 (0.96-1.4, p = 0.11).

In other words, at the time of this interim analysis, this trial was neither able to detect clear benefit or harm for any of the aforementioned antivirals in preventing in-hospital mortality *or* shortening the duration of symptoms. In subgroup analyses stratified by patient age and oxygen needs for each antiviral, no clear benefit was noted for any of the antivirals. Furthermore, there was no evidence that remdesivir prevented progression of disease in those without oxygen needs at the time of enrollment. Signals of potential *harm* leading to death were noted in the subgroup analyses for HCQ, specifically for patients aged 50-69 years of age.

How does this study fall in line with ACTT-1 trial of remdesivir, which we have covered before? (ACTT-1 was the study of patients randomized to placebo or remdesivir, which showed no mortality benefit, though a shorter duration of symptoms among those who recovered). The authors of Solidarity included a meta-analysis as part of their interim results, which included ACTT-1, a trial conducted in Wuhan, the SIMPLE trial, in addition to the Solidarity data. They found that for patients *not on mechanical ventilation*, remdesivir did not improve mortality. The death ratio for this group was 0.80 (0.63-1.01) which is at least a *signal* for benefit given the vast majority of entirety of the 95% confidence interval falls on the side of “favor”.

So, does remdesivir improve overall mortality in patients hospitalized with covid-19? The answer is still likely no. But might there a group of patients who may benefit from it? It’s possible that those patients hospitalized with covid-19 who have less severe disease might benefit. But the evidence is not definitive, and overall unimpressive. We eagerly await the final report of the Solidarity trial.

—Joshua Niforatos, MD

POLICY BRIEFING

Why is the Trump administration so “e-mask-ulated”?

Early in the pandemic, some public health officials and experts downplayed the importance of wearing masks among members of the public. There were two main reasons for this. The first is related to SARS-CoV-2 being thought of as a “respiratory pathogen.” Most such viruses and bacteria do not typically spread in asymptomatic people. This means that until symptoms occur, the risk of spread is slim-to-none for most diseases such as influenza and a variety of pathogens that cause flu-like illnesses. The thought was that if people were not having symptoms, they could go about their business and not spread it to others. Once the extent of symptom-free contagion became clear, the idea of covering the mouths and noses of people who may not know they are infected began to make more sense.

The second is that early in the United States outbreak, there was a national run on N95 masks. Unlike cloth coverings and even surgical masks, N95 masks (known as respirators) were known both to decrease the spreading of disease from a contagious person as well as intercepting droplets headed towards the noses and mouths of uninfected persons. So when the public started buying these masks in droves, the fear was the healthcare professionals, those who were most likely to be exposed to people with the virus, would not have enough. Amazon had to crack down on price gouging of the masks (and also prioritized hand sanitizer orders to medical facilities) early in the pandemic. Many experts, myself included, worried that public hoarding of personal protective equipment would leave us in the medical profession unable to perform our duties safely.

While there are still semantic debates as to the extent that SARS-CoV-2 is “airborne,” most experts now agree that the largest fraction of spread is not from surfaces as we once believed, but through droplets in the air, whether from people very close by or—in the right circumstances—those recently in the room.

So why have members of the Trump administration and its acolytes and bootlickers resisted wearing them? Over the weekend, Scott Atlas, President Trump’s current favorite medical doctor without the requisite experience or judgment to make credible or cogent covid-19 policy, tweeted inaccurate statements about masks. Twitter removed the tweet for violating its terms of use on medical misinformation. Meanwhile, former New Jersey Governor Chris Christie has admitted that he should have worn a mask while working in the White House late last month, where it is thought he acquired covid-19, leading to a nearly week-long hospitalization.

There seems to be a mythology among some that somehow masks might be dangerous. As we have [covered](#) in *Brief19*, even among persons with existing lung disease such notions are ludicrous. Meanwhile, masks [decrease](#) spread of coronaviruses from a small (6 percent) to a great extent (80 percent), especially combined with [practices](#) such as physical distancing and hygiene. This implies that many lives would be saved if mask use rates were higher.

Perhaps it all comes back to an observation made early in the pandemic; men are [less likely](#) to wear masks. More recently, President Trump insulted Vice President Biden for wearing masks *too often*. Could it be that the male ego among some of our leaders is so fragile that it can be derailed by a piece of cloth? Ironically, nothing could project weakness any more effectively than cowering in fear over something as benign—not to mention as helpful—as PPE.

—Jeremy Samuel Faust MD, MS

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