

## **BRIEF19**

*A daily review of covid-19 research and policy.*

### **RESEARCH BRIEFING**

**Dexamethasone appears to be first drug shown to reduce covid-19 deaths.** Dexamethasone, an inexpensive steroid that is widely available appears to be the first medication shown in a high-quality study to reduce the rate of death in any subset of covid-19 patients. After a press release last week announced that patients on mechanical ventilators in particular survived substantially more often than those who did not, many experts called for the immediate release of more data. Today, a substantial amount of data from the study [was posted](#) on medRxIV; the paper has not yet undergone peer review. The results come from a larger conglomerate of trials being conducted in the U.K. known as the Recovery Trial. The data shared today showed that the primary outcome of the study--death rate among subjects 28 days after entering the study--was significant; 21.6% of patients who were randomly selected to receive dexamethasone were dead at 28 days versus 24.6% among patients who received all other aspects of intensive care, but not dexamethasone. This suggests that 20 patients would need to receive the drug for one life to be saved. However, the researchers previously planned to analyze the results of patients who were already on mechanical ventilators at the time they entered the study, those requiring oxygen (but not in comas on ventilators), and those without either requirement. Among those groups, those on mechanical ventilators had by far the greatest effect: 40.7% of patients who did not receive the drug had died by day 28 compared with 29% among those who did. A reduction in deaths of over 11% is not only an unusually large effect for an ICU study of any kind. Patients who needed oxygen only (but were not in comas on ventilators) also fared better, dying 21.5% of the time versus 25% among controls. However, among patients who did not require any oxygen, dexamethasone did not help, and in fact, more patients in that group who received the drug died, though the increase was not statistically significant. Whether the extra 11% of patients who survived to day 28 among patients on ventilators had improved enough so as to be awake was not reported in the manuscript. The document will require peer review and there are several areas of the paper that are incomplete, a reflection of the speed with which the document was prepared over the last week or so. *Abbreviated from Brief19 for [23 June 2020](#).*

*–Jeremy Samuel Faust MD, MS*

**An old drug, colchicine may help covid-19 patients.** The search for therapies to treat covid-19 has intensified. Anti-inflammatory compounds are now being closely considered. Such medications might be effective because the body's over-exuberant inflammatory response to SARS-CoV-2 is thought to be responsible for some of the health problems associated with covid-19. Steroids, like dexamethasone, are potent anti-inflammatories, but even short courses of steroids can have important side effects. The authors of a [new study](#) appearing in *JAMA Network Open* conducted a clinical trial to investigate whether colchicine had similar benefits to dexamethasone against SARS-CoV-2, though perhaps without its common side effects. The study was not blinded meaning that while subjects were chosen at random to either receive colchicine or not, both the patients and the researchers were aware of which patients received the drug. Colchicine is approved by the FDA to treat gout flares, though it has other "off-label" uses for conditions including difficult to control arthritis. Colchicine works by blocking the lifecycle of cells; it prevents cells from fully functioning by binding to tiny structures within cells called microtubules. In certain types of cells, colchicine inhibits the release of inflammatory chemicals. In [a study](#) of 105 patients who were hospitalized for covid-19, researchers primarily studied whether colchicine had any impact on blood markers of stress and inflammation as well as clinical outcomes. There was no difference in the blood tests between the groups (cardiac troponin and c-reactive protein). However, patients who received colchicine were more likely to have clinical improvements, as

determined by a 7-grade numerical scale recommended by the World Health Organization for assessing patient outcomes in covid-19 drug trials. A score of 1 means that a patient can walk or do their usual activities; 6 corresponds to requiring invasive mechanical ventilation or lung bypass (ECMO); 7 is death. 14% of patients who received colchicine improved by two or more points on the scale, compared to just 1.8% of patients among the control group. The researchers also found no patients who received colchicine required mechanical ventilation, versus three among those who had not received colchicine. However, the number of deaths was similar between the groups. Patients in the group that did not receive colchicine were found to have, on average, higher concentrations of d-dimer in their blood, another marker of systemic inflammation. With regard to side effects, those receiving colchicine had more diarrhea. These results are preliminary. The study was small and, as described here, used what are called “composite endpoints” and arbitrary scales. These methods make it difficult to tease out which of the outcomes may have been directly affected by the drug. Also, the lack of blinding introduces substantial bias, especially in the context of the hope invested in finding a successful treatment for covid-19. These issues aside, it is encouraging to see researchers exploring repurposing low-cost and well-understood drugs, which, if found to be beneficial, are already likely to be readily accessible around the world. *Abbreviated from Brief19 for 25 June 2020.* –Michael Chary, MD PhD

**Covid-19 and mental health. Can telemedicine help?** The pandemic has resulted in unprecedented measures in many parts of the world aimed at preventing the transmission and spread of SARS-CoV-2. While many of these measures, such as social distancing and reduction of mass gatherings, have contributed to the reduction of the disease transmission, the behavioral and psychological consequences may be significant. A [new article](#) in *JAMA Psychiatry* discusses many of the psychological challenges generated by covid-19. Based on previous large-scale outbreaks of the Ebola virus disease from 2014 to 2016, we know that anxiety, posttraumatic stress disorder and depression is likely to be common amongst survivors. Data from the covid-19 pandemic already indicates alarmingly high rates of depression and acute stress amongst both survivors and healthcare providers. This is further exacerbated by the fact that many mental health services have been limited or severely restricted due to the closing of outpatient clinics. However, covid-19 is occurring during an historic period of digital integration throughout society. While screens that offer a constant stream of never-ending news cycles and social media saturation may add represent additional stressors, these same technologies also offer opportunities for timely screening and early intervention by healthcare providers for patients with access. Telemedicine platforms may substantially enhance mental health support structures during this period. Additionally, the use of social media platforms among friends, families, and close contacts may aid in maintaining networks of support and connectedness during prolonged periods of social restrictions. The development of online programs may facilitate remote behavioral interventions. One area not discussed in the article, however, is that of unequal access to online services. High speed reliable internet should not be taken for granted in many parts of the country and around the world. In areas where access to adequate internet services are limited, online mental healthcare may not reach populations most likely to benefit from them. Addressing these disparities should be a priority for public health officials. *26 June 2020.* –Bernard Chang MD

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*Brief19* is a daily executive summary of covid-19-related medical research, news, and public policy. It was founded and created by frontline emergency medicine physicians with expertise in medical research critique, health policy, and public policy.