Happy Veterans Day! This is a federal holiday for America to celebrate those who served honorably in the military. The day was first recognized as Armistice Day in 1919 to celebrate the end of World War I and became Veterans Day in 1954. Like most celebrations in 2020, Veterans Day will look different due to COVID-19!

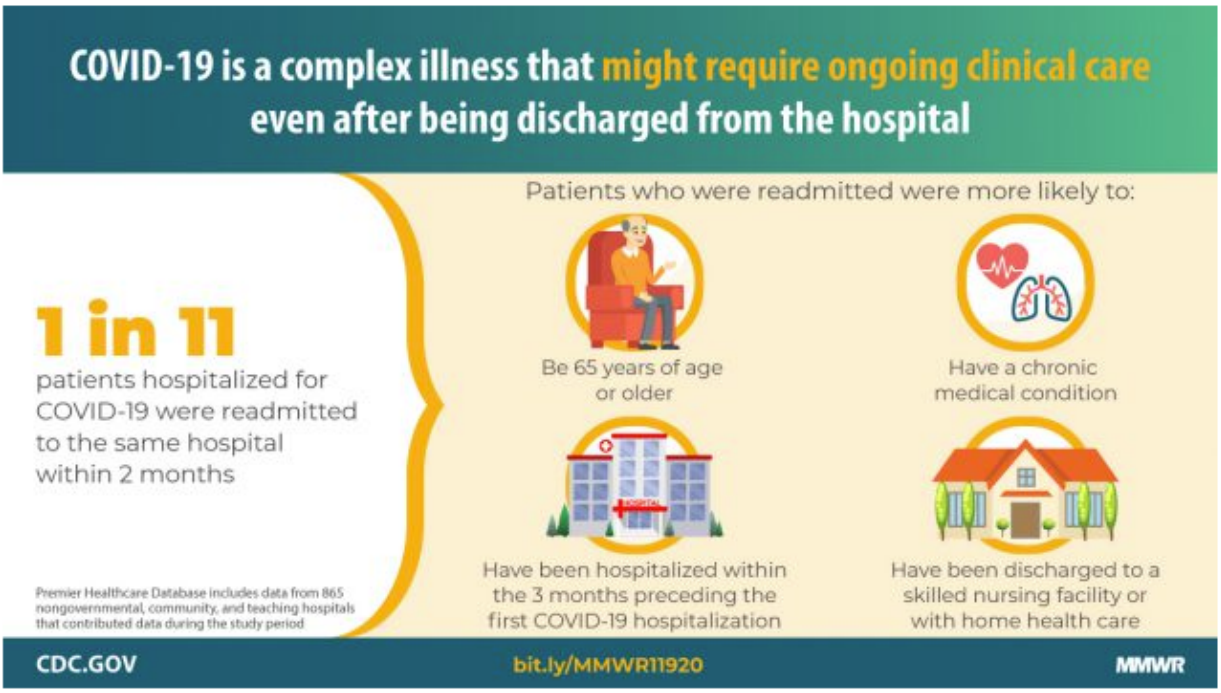
First as most of you have heard, the FDA has granted EUA for Eli Lilly's monoclonal for people 12 and older with mild or moderate COVID-19 not requiring hospitalization. It is a one-time treatment given through an IV. I assume Regeneron will not be far behind. Second is the announcement that Pfizer's vaccine has showed in an early analysis to be more than 90% effective in protecting people from Covid-19, a much-better-than-anticipated result. This is a 2-dose vaccine which uses a new technology, known as mRNA. Moderna's vaccine also uses the mRNA technology.

Next, today's Daily Briefing looks at the important question of readmissions in the US. The second article looks at use of ivermectin as an antiviral to treat SARS-CoV-2 which has not received much attention in the Daily Briefing. The last article is another well done negative trial evaluating HCQ. As I point out there are lessons learned. Looking ahead to Friday's Daily Briefing I will review articles on risk of indoors and another study reviewing why young children appear to have lower risk of infection with SARS-CoV-2 so stay tuned!

Ed

Characteristics of Hospitalized COVID-19 Patients Discharged and Experiencing Same-Hospital Readmission — United States, March–August 2020
MMWR published November 9, 2020, article submitted by John Butler
https://www.cdc.gov/mmwr/volumes/69/wr/mm6945e2.htm?s_cid=mm6945e2_w
CDC investigators used electronic health record and administrative data from the Premier Healthcare Database. They assessed patterns of hospital discharge, readmission, and demographic and clinical characteristics associated with hospital readmission after a patient's initial COVID-19 hospitalization (index hospitalization). Among 126,137 unique patients with an index COVID-19 admission during March–July 2020, 15% died during the index hospitalization.

Among the 106,543 (85%) surviving patients, 9% (9,504) were readmitted to the same hospital within 2 months of discharge through August 2020. Readmissions occurred more often among patients discharged to an SNF (15%) or those needing home health care (12%) than among patients discharged to home (7%). The odds of hospital readmission increased with age among persons aged ≥65 years, presence of certain chronic conditions, hospitalization within the 3 months preceding the index hospitalization, and if discharge from the index hospitalization was to an SNF or to home with health care assistance.



Comments: These results support recent analyses that found chronic conditions to be significantly associated with hospital readmission [Int J Clin Pract 2020;00:e13700] and could be explained by the complications of underlying conditions in the presence of COVID-19, COVID-19 sequelae, or indirect effects of the COVID-19 pandemic. Understanding the risk factors can inform clinical practice, discharge disposition decisions, and public health priorities such as health care planning to ensure availability of resources needed for acute and follow-up care of COVID-19 patients. Chronic conditions were identified using ICD-10-CM diagnostic codes used at the index hospitalization or a previous encounter. If a patient had a chronic condition but the condition was not assigned a diagnostic code, that condition would not be captured in this analysis. In addition, primary discharge diagnosis was used to infer the primary reason for hospital admission; other diagnoses might have contributed to the reason for index admission and readmissions.

Use of Ivermectin Is Associated with Lower Mortality in Hospitalized Patients with Coronavirus Disease 2019

Chest published online October 12, 2020

doi.org/0.101/j.chest.2020.10.009

Ivermectin has been shown to inhibit SARS-CoV-2 in vitro. Patients were put into two groups: ivermectin vs usual care. Patients in the ivermectin group received at least one oral dose of ivermectin at 200 mg/kg in addition to usual clinical care. A second dose could be given at the discretion of the treating physician at day 7 of treatment. The decision to prescribe ivermectin, hydroxychloroquine, azithromycin, or other medications was at the discretion of the treating physicians. Propensity score matching created a total of 98 matched pairs. After matching, no statistically significant differences were found between the two groups.

In a multivariable-adjusted analysis, mortality was significantly lower in patients treated with ivermectin compared with those not treated with the drug. In addition, mortality rates were significantly lower in a subgroup of patients with pulmonary involvement who were treated with ivermectin compared with similar patients not treated with the drug (38.8% vs 80.7%, respectively).

Comment: This study has limitations. Because of the retrospective observational nature of the study, despite adjustment for known confounders and propensity score matching, they cannot exclude the possibility of unmeasured confounding factors. Clearly more trials are needed, but results are intriguing.

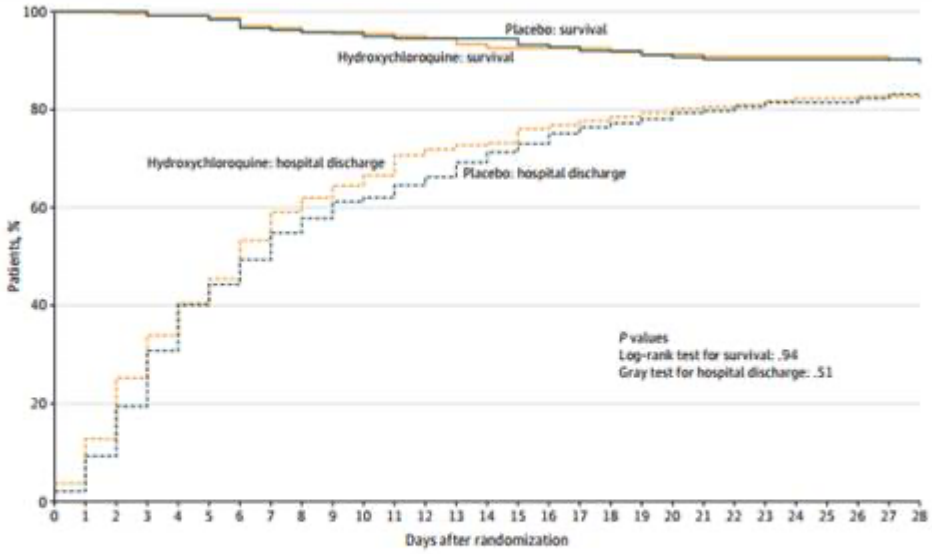
Effect of Hydroxychloroquine on Clinical Status at 14 Days in Hospitalized Patients With COVID-19: A Randomized Clinical Trial

JAMA published online November 9, 2020
doi:10.100/jama.2020.22240

This was a multicenter, blinded, placebo-controlled randomized trial conducted at 34 hospitals in the US. Adults hospitalized with respiratory symptoms from severe acute respiratory syndrome coronavirus 2 infection were enrolled between April 2 and June 19, 2020, with the last outcome assessment on July 17, 2020. The planned sample size was 510 patients, with interim analyses planned after every 102 patients were enrolled. Patients were randomly assigned to hydroxychloroquine (400 mg twice daily for 2 doses, then 200 mg twice daily for 8 doses) (n = 242) or placebo (n = 237). The primary outcome was clinical status 14 days after randomization as assessed with a 7-category ordinal scale ranging from 1 (death) to 7 (discharged from the hospital and able to perform normal activities). The primary outcome was analyzed with a multivariable proportional odds model, with an adjusted odds ratio (aOR) greater than 1.0 indicating more favorable outcomes with hydroxychloroquine than placebo. The trial included 12 secondary outcomes, including 28-day mortality.

Among 479 patients who were randomized (median age, 57 years) 20.1% in the intensive care unit; 46.8% receiving supplemental oxygen without positive pressure; 11.5% receiving noninvasive ventilation or nasal high-flow oxygen; and 6.7% receiving invasive mechanical ventilation or extracorporeal membrane oxygenation). 90% completed the primary outcome assessment at 14 days. The median duration of symptoms prior to randomization was 5 days (interquartile range [IQR], 3 to 7 days). [most trials have had difficulty capturing duration of symptoms] Clinical status on the ordinal outcome scale at 14 days did not significantly differ between the hydroxychloroquine and placebo groups (median [IQR] score, 6 [4-7] vs 6 [4-7]; aOR, 1.02 [95% CI, 0.73 to 1.42]). None of the 12 secondary outcomes were significantly different between groups. At 28 days after randomization, 25 of 241 patients (10.4%) in the hydroxychloroquine group and 25 of 236 (10.6%) in the placebo group had died (absolute difference, -0.2% [95% CI, -5.7% to 5.3%]; aOR, 1.07 [95% CI, 0.54 to 2.09]). The trial was stopped at the fourth interim analysis for futility with a sample size of 479 patients.

Figure 3. Survival and Hospital Discharge Through 28 Days Following Randomization



Survival																												
Hydroxychloroquine	241		241	240		239	238	234	233	231		230	229	228	225			223	221		220						219	216
Placebo	236			236		234	232	228	227		226	224				223	220	219		217	215	214						213
Discharge																												
Hydroxychloroquine	242	233	211	180	158	142	129	106	92	84	77	72	61	57	53	50	43	41	39	35	32	30	28	27	25		24	23	21
Placebo	237	232	215	191	162	140	128	113	99	91	83	79	72	68	61	56	50	44	39	37	34	30	28	26			24	22	20

Comment: This is another study that confirms several recently published studies which demonstrated similar findings. In robust well-conducted clinical trials published to date hydroxychloroquine has been evaluated in a wide variety of populations, ranging from patients with severe illness to individuals at risk of SARS-CoV-2 infection, in whom the drug was used as primary prophylaxis. All these studies failed to show any beneficial effect of the drug.

Patients who have a potentially life-threatening disease are desperate and will accept any treatment that appears to be effective which occurred early in this pandemic. Nonrandomized studies must be considered preliminary and not standard of care. Second, leaders from the NIH, physician organizations and societies, pushed back and resisted being forced to promote the politically motivated use of hydroxychloroquine. They should be recognized for their commitment to science over politics. I hope we have all learned valuable lessons as we continue to evaluate new therapeutics and how best to use the therapeutics we already have like remdesivir and convalescent plasma.