The following summarizes key literature pertaining to treatment of COVID-19 during the past week. *Note: some of the data discussed below is in pre-print form that has not yet been peer-reviewed. We have noted some discrepancies in some of this data, and final printed versions may ultimately differ from what is shown here. We will update as soon as possible; caution is advised when interpreting this literature.

**Vaccine Publication**

Earlier this week, preliminary results of the initial studies of the Moderna mRNA vaccine were published in the *New England Journal of Medicine*—this initial experience in 45 patients was promising with all demonstrating some degree of immune response. This is a preliminary finding, however and we eagerly await the larger Phase III studies which are set to begin later this month. [https://www.nejm.org/doi/full/10.1056/NEJMoa2022483](https://www.nejm.org/doi/full/10.1056/NEJMoa2022483)

**Treatment Updates**

*NIH Guideline Update- 7-17-2020*

Today, the NIH treatment guideline was updated in several aspects. The summary with links to the guideline can be found at this site: [https://www.covid19treatmentguidelines.nih.gov/whats-new/](https://www.covid19treatmentguidelines.nih.gov/whats-new/)

Updated information includes:

- Remdesivir: Provides clarification for allocating remdesivir in areas where supplies are limited. Suggests prioritizing for patients who are hospitalized and require supplemental oxygen but not mechanical ventilation or ECMO.
- Corticosteroids: Previous recommendations from 6/25/20 were added to the immunomodulator section (no change in the guidelines for use).
- New sections:
  - Mesenchymal stem cell: Panel recommends against use outside of clinical trial
  - Vitamin C: insufficient data to recommend either for or against use of vitamin C in non-critically ill patients
  - Vitamin D: insufficient data to recommend either for or against the use of vitamin D for the prevention or treatment of COVID-19
  - Zinc: insufficient data to recommend either for or against the use of zinc for the treatment of COVID-19 and panel recommends AGAINST use of zinc supplementation above the recommended daily allowance for prevention of COVID-19 outside of a clinical trial
  - Special considerations in solid organ transplant, stem cell transplant and cellular therapy candidates, donors and recipients
  - Additional updates to available clinical trials for other sections no changing recommendations
**Remdesivir** - DHHS has launched a new tracking page to share information on the allocation process for the commercial remdesivir supply. North Carolina did not receive additional supplies in this allocation. This page can be found at this link: [https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/remdesivir.aspx](https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/remdesivir.aspx)

**New Literature This Week**

*Dexamethasone*


This is the publication of data previously discussed in a June 17th press release and a pre-print posted on June 22nd that was published in the *New England Journal of Medicine* on July 17th. This was previously discussed in the DASON Literature Update on 6/26/2020 ([https://dason.medicine.duke.edu/sites/dason.medicine.duke.edu/files/dason_weekly_update_6-26.pdf](https://dason.medicine.duke.edu/sites/dason.medicine.duke.edu/files/dason_weekly_update_6-26.pdf)) when the NIH guidelines were updated. Overall the main conclusions do not change and we will be preparing an FAQ on dexamethasone considerations in the coming week.

*Hydroxychloroquine*


This was a randomized, double-blind, placebo controlled trial of symptomatic non-hospitalized adults with a confirmed positive SARS-CoV-2 test or high-risk exposure within 4 days of symptom onset. Participants were from the US and Canada, with the coordinating center at University of Minnesota. 56% of participants were enrolled within one day of the start of symptoms. Subjected received hydroxychloroquine (HCQ) (800 mg x1, followed by 600 mg 6-8h later, then 600 mg QD x 4 days) or placebo tablets. Baseline and follow-up data from each participant were collected via electronic surveys. Median age of study participants was 40 years (IQR 32-50 years) and 56% were women. Only 3% self-identified as Black/African-American. The primary outcome was originally planned to be based on hospitalization or death, but this was found to be much lower than expected in a blinded interim analysis of study data; this was thus modified to change in overall symptom severity over 14 days based on a 10-point visual analog scale. 98% of participants had at least one symptom at baseline, and a median of 4 symptoms [IQR 2-6 symptoms]. There was no difference in change in symptom severity over 14 days in the two groups. HCQ patients had a mean reduction of 2.60 points from baseline, compared to a 2.33-point reduction in the placebo group (-0.27 points [95% CI -0.6100.07 points]). This result did not change when assessed according to many pre-specified subgroups. At day 5, symptoms were present in 54% and 56% of the HCQ and placebo patients, respectively. At day 14 this was 24% (HCQ) and 30% (placebo), p=0.21. Incidence of hospitalization or deaths was 3.2% overall, and not different between groups (p=0.29). Adverse effects (predominantly GI complaints) were significantly higher among those receiving HCQ (43%) vs placebo (22%), p<0.001. Concomitant zinc or vitamin C was taken by study participants (~31% and 49% of HCQ participants, respectively) and did not significantly improve symptoms compared to HCQ alone. Potential limitations of this study include the fact that all evaluations were self-reported by study participants, only 58% of study participants had COVID testing performed, and lack of laboratory/viral loads monitoring due to the remote nature of the study participants. EKGs were not performed or reported by the investigators.

An commentary has been published on this paper as well, discussing strengths and limitations of the study: Schluger NW. The saga of hydroxychloroquine and COVID-19: a cautionary tale. Annals of Internal Medicine, 2020. [https://doi.org/10.7326/M20-5041](https://doi.org/10.7326/M20-5041)
This was a multicenter, open label, randomized controlled trial of nonhospitalized adults with a confirmed positive test for SARS-CoV-2 enrolled within 5 days of symptom onset in Catalonia, Spain. Subjects received either HCQ (800 mg x1, followed by 400 mg QD for 6 days) or standard of care (SOC). Initially, subjects also received darunavir/cobicistat with HCQ but this was discontinued during enrollment due to emerging data demonstrating lack of in vitro activity of DRV/c against SARS-CoV-2. Participants had a mean age of 41.6 years and ~69% were women. Median time from onset of symptoms to enrollment was 3 days [IQR 2-4 days]. There were no significant differences in the primary outcome of change in viral load from baseline at day 3 for HCQ (-1.41 log10 copies/ml) vs SOC (-1.41 log10 copies/ml) or day 7 (-3.37 HCQ vs -3.44 SOC log10 copies/ml). No differences in viral responses were apparent for patients that did or did not receive DRV/C with HCQ. There were no significant differences in hospitalization (5.9% HCQ vs 7.1% SOC, RR 0.75 [95% CI 0.32, 1.77]) or mean time to symptom resolution from randomization (10 days HCQ [IQR 4-18] vs 12 days SOC [IQR 6-21], p=0.38. However, there were significantly more AEs with HCQ (72%) vs SOC (9%), but these were mostly mild-moderate GI symptoms or complaints such as drowsiness, headache, or metallic taste. There were no deaths in either study group. Limitations of this trial include lack of placebo, change in the active treatment during the study, and overrepresentation of health care workers in the study (>80% of participants).

Treatment Summary Tables

The remdesivir summary table with the information of published studies to date can be found at this link: https://dason.medicine.duke.edu/summary-recent-clinical-data-use-remdesivir-covid-19

The hydroxychloroquine summary table is available at this link: https://dason.medicine.duke.edu/summary-recent-clinical-data-use-hydroxychloroquine-and-chloroquine-covid-19

The tocilizumab summary table with the information of published studies to date can be found at this link: https://dason.medicine.duke.edu/summary-recent-clinical-data-use-tocilizumab-covid-19

Updated FAQs