

Response to: “Overcoming the therapeutic nihilism of out-of-hospital management of COVID-19 patients”

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Running Head: Overcoming Covid-19 Therapeutic Nihilism

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I thank Dr. Meini for his discussion (1) of exactly the problem that we have faced in management of pandemic COVID-19 in the industrialized countries: not only the ignoring, but the misrepresentation of early outpatient treatment as not beneficial or as harmful (2). Thus, the “sicken-in-place” formal position of the NIH (3): stay home without treatment until you can’t breathe, then go to the emergency room. It is no longer only disparagement against hydroxychloroquine (HCQ); NIH has also made recommendations against outpatient use of ivermectin and of all steroid use (4), their discussions ignoring the substantial published evidence of outpatient benefit. For example, in spite of the fact that the outpatient randomized controlled trials of HCQ were terminated early thereby reducing their statistical power, taken as a whole they clearly demonstrate statistically significant reduction in risks of hospitalization, mortality or new infection (5). Both separate from and along with the HCQ benefit, prednisone starting symptom day-6 has shown significant reduction in risk of hospitalization (6). The largest nonrandomized but controlled outpatient trial, of HCQ+zinc versus zinc alone, conducted as a national study in the modernized healthcare system across the entire country of Saudi Arabia and including nearly 8,000 patients, showed a dramatic and very significant 4-5-fold mortality reduction in the HCQ+zinc arm (7). Worldwide, countries using HCQ or ivermectin as the basis component for early outpatient treatment have per capita COVID-19 mortality proportions 4-fold or more lower than the US (8,9).

Common sense tells us that HCQ is exceedingly safe. It has been safely used for 65 years by hundreds of millions of people in tens of billions of doses worldwide, prescribed without routine screening EKGs, given to adults, children, pregnant women and nursing mothers, thus must be safe when used in the initial viral-replication phase of an illness that is similar at that point to colds or flu. Same for ivermectin. The University of Oxford study showed that in 14 large

international medical-records databases of older rheumatoid arthritis patients, no significant differences were seen in all-cause mortality between patients who did or did not use HCQ (10,11). The Oxford investigators also looked at cardiac arrhythmias and their data show no increases among the more than 900,000 HCQ users (11). This fact is completely consistent with the established medical literature for HCQ (12).

The common consensus of physicians who actually treat COVID-19 outpatients, as opposed to ivory-tower academics and other doctors who treat hospitalized patients and have no experience with outpatients, is an immediate, staged, multi-drug approach (13) very similar to the one outlined by Dr. Meini. Outpatient treatment is not “all about HCQ,” it is finding the combination and sequence of medications that is optimal for the specific patient. In delivering this care, physicians must be able to recommend and patients free to choose courses of treatment from within all approved medications, based on best available applicable evidence, without the absurd, money-driven corrupted meddling and restrictions of government bureaucracies as suffered in many of the western nations (14).

References

1. Meini S. Overcoming the therapeutic nihilism of out-of-hospital management of COVID-19 patients. *Am J Epidemiol* 2020 xxxx###.
2. Woodworth E. The Media Sabotage of Hydroxychloroquine Use for COVID-19: Doctors Worldwide Protest the Disaster. Media and Big Pharma are in lockstep to suppress a cheap, life-saving Covid-19 therapy in order to reap pandemic-sized profits. June 30, 2020. Accessed July 2, 2020. <https://www.globalresearch.ca/media-sabotage-hydroxychloroquine-covid-19-doctors-worldwide-protest-disaster/5717382>

3. NIH COVID-19 Treatment Guidelines. Therapeutic Management of Patients with COVID-19. Last Updated: October 9, 2020. Accessed November 23, 2020. <https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/>
4. NIH COVID-19 Treatment Guidelines. Antiviral Drugs That Are Approved or Under Evaluation for the Treatment of COVID-19. Last Updated: November 3, 2020. Accessed November 23, 2020. <https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/>
5. Ladapo JA, McKinnon JE, McCullough PA, Risch HA. Randomized controlled trials of early ambulatory hydroxychloroquine in the prevention of COVID-19 infection, hospitalization, and death: meta-analysis. Preprints September 30, 2020. <https://www.medrxiv.org/content/10.1101/2020.09.30.20204693v1>
6. Szente Fonseca SN, de Queiroz Sousa A, Wolkoff AG, et al. Risk of hospitalization for Covid-19 outpatients treated with various drug regimens in Brazil: Comparative analysis. *Travel Med Infect Dis* 2020;38:101906. <https://doi.org/10.1016/j.tmaid.2020.101906>
7. Sulaiman T, Mohana A, Alawdah L, et al. The effect of early hydroxychloroquine-based therapy in COVID-19 patients in ambulatory care settings: A nationwide prospective cohort study. Preprints September 13, 2020. <https://doi.org/10.1101/2020.09.09.20184143>
8. HCQ Trial. Early treatment with hydroxychloroquine: a country-based analysis. *Covid Analysis*, August 5, 2020 (Version 35, November 14, 2020). Accessed November 30, 2020. <https://hcqtrial.com/>
9. HCQ Meta. HCQ is effective for COVID-19 when used early: analysis of 150 studies. *Covid Analysis*, October 20, 2020 (Version 24, November 29, 2020). Accessed November 30, 2020. <https://hcqmeta.com/>

10. Lane JCE, Weaver J, Kostka K, et al. Risk of hydroxychloroquine alone and in combination with azithromycin in the treatment of rheumatoid arthritis: a multinational, retrospective study. *Lancet Rheumatol* 2020;2:e698-711. [https://doi.org/10.1016/S2665-9913\(20\)30276-9](https://doi.org/10.1016/S2665-9913(20)30276-9)
11. Risch HA. Early outpatient treatment of symptomatic, high-risk COVID-19 patients that should be ramped up immediately as key to the pandemic crisis. *Am J Epidemiol* 2020;189(11):1218-1226. <https://doi.org/10.1093/aje/kwaa093>
12. Fram G, Wang DD, Malette K, et al. Cardiac complications attributed to hydroxychloroquine: A systematic review of the literature pre-COVID-19. *Curr Cardiol Rev* 2020;16:1-9. <https://doi.org/10.2174/1573403X16666201014144022>
13. McCullough PA, Kelly RJ, Ruocco G, et al. Pathophysiological basis and rationale for early outpatient treatment of SARS-CoV-2 (COVID-19) infection. *Am J Med* 2020 August 6, in press. [https://www.amjmed.com/article/S0002-9343\(20\)30673-2/](https://www.amjmed.com/article/S0002-9343(20)30673-2/)
14. Todaro JM. Gilead: Twenty-one billion reasons to discredit hydroxychloroquine. *OmniJournal* July 23, 2020. Accessed November 30, 2020. [https://omnij.org/Gilead: Twenty-one billion reasons to discredit hydroxychloroquine \(ORIGINAL ARTICLE\)](https://omnij.org/Gilead: Twenty-one billion reasons to discredit hydroxychloroquine (ORIGINAL ARTICLE))