Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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The Reply

We respectfully join Dr. Weissmann and colleagues in a call for large high-quality randomized trials in coronavirus disease (COVID-19). This potentially fatal viral illness requires multiple drugs from different therapeutic categories to successfully manage, preferably on an ambulatory basis and not during a hospitalization. Unfortunately, in our view[1] there are no conclusive randomized trials of either single or more appropriately multiple drugs with double dummies in ambulatory patients. To our knowledge, no such trials are forthcoming. Thus, we must act on clinical judgment supported by our understanding of pathophysiology, and the totality of evidence concerning therapy.[2] Since the time of the original publication in ***The American Journal of Medicine***, we have updated the treatment algorithm to include bamlanivimab, casirivimab and imdevimab, and ivermectin (Figure).[2]

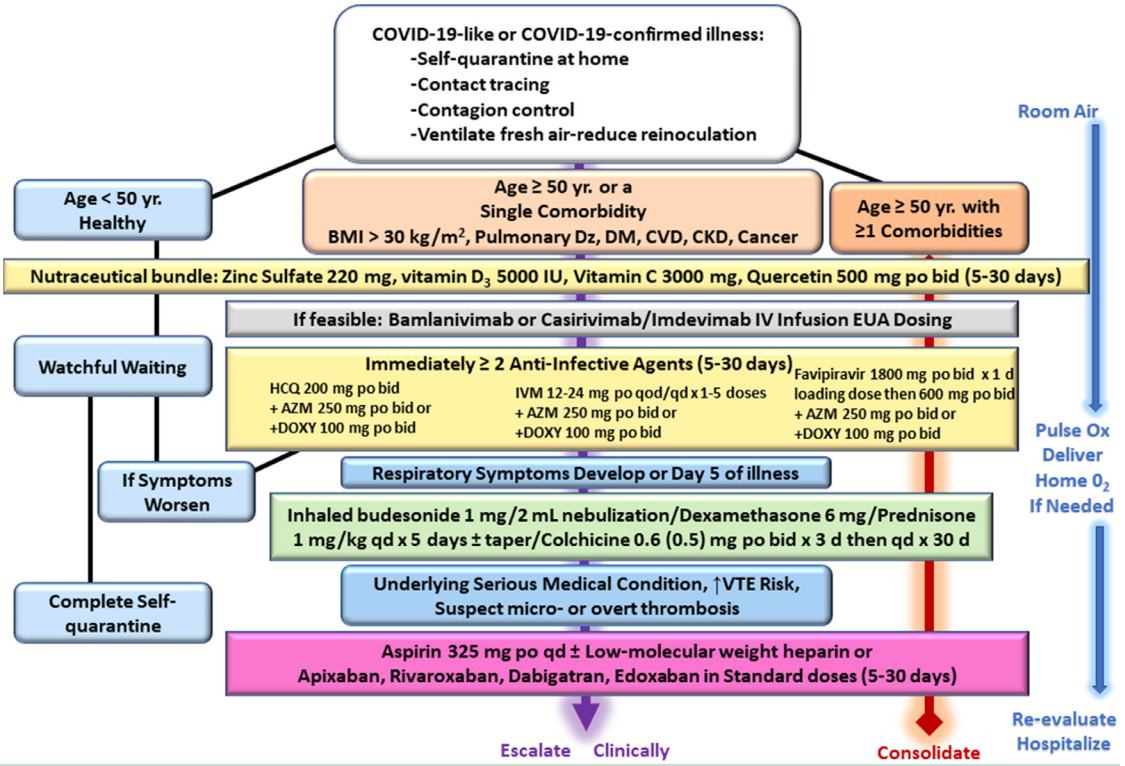

Figure Sequential multidrug treatment algorithm for ambulatory acute COVID-19-like and confirmed COVID-19 illness in patients in self-quarantine. AZM = azithromycin; BMI = body mass index; CVD = cardiovascular disease; CKI = chronic kidney disease; DM = diabetes mellitus; DOXY = doxycycline; Dz = disease; EUA = Emergency Use Authorization (USA); HCQ = hydroxychloroquine; IVM = ivermectin; Mgt = management; Ox = oximetry; VTE = venous thromboembolism. Reproduced with permission from McCullough et al.[2]

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Oral steroids are now better supported by multiple trials and observational studies, including the use of prednisone.[3,4] The rationale for either azithromycin or doxycycline to complete a pair of oral, intracellular antiinfective agents remains unchanged.[2] Finally, since the time of our original publication, early ambulatory treatment has become an emerging standard in over 30 countries, including several states in Brazil where home treatment kits are utilized relying upon the principles we have published.[2] We invite Dr. Weissman and colleagues to join us in breaking therapeutic nihilism toward ambulatory patients with COVID-19—this has led to catastrophic levels of fear, suffering, hospitalization, and death. Sources of real-word data suggest early ambulatory sequenced multidrug therapy is associated with ~85% reductions in morbidity and mortality due to COVID-19 with no signals of harm.[2,5,6,7]

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