Early ambulatory multidrug therapy for SARS-CoV-2 (COVID-19) infection.

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Abstract

SARS-CoV-2 infection (COVID-19) illness involves viral mediated organ damage, cytokine storm, and thrombosis. Once ill, the only method of reducing the risk of hospitalization and death is medical treatment in the ambulatory phase using the same principles for hospitalized patients. Early therapy that has a reasonable chance of success and an acceptable safety profile includes: 1) combination antiviral therapy, 2) corticosteroids, 3) antiplatelet agents/antithrombotics, 4) supportive care including supplemental oxygen, monitoring, and telemedicine. The current rates of hospitalization and death are unacceptably high under the present paradigm of contagion control and watchful waiting for a vaccine.
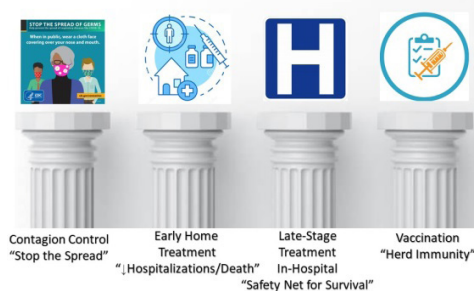
Description

The SARS-CO-V2 (COVID-19) global crisis has driven considerable efforts on pandemic response (Figure 1) which can be viewed as having four pilars: 1) contagion control, 2) early ambulatory treatment to reduce hospitalization and death, 3) hospitalization as a safety net to save lives at the critical stage, and 4) herd immunity through vaccination and prior COVID-19 illness. Unfortunately efforts at contagion control have failed, hospitalization is not an adequate safety net, and vaccination is not currently available [1].


Figure 1. Four pilars of pandemic response.

Across the globe we must turn our attention to the least emphasized pilar of early ambulatory treatment [2]. There are a wide range of responses on early treatment to multi-drug home treatment kits in deployed in countries such as India, Brazil, Guatemala, and Salvador to near complete prohibition of ambulatory treatment in the U.S., Canada, United Kingdom, Western European Union, and Australia [3]. Penalties for an Australian physician who attempts to prescribe a therapy such as hydroxychloroquine in an acutely ilxl COVID-19 patient can include imprisonment [4]. Never has

modern medicine witnessed such disparate courses of action for doctors and patients. After approximately ~50,000 publications on COVID-19 cited in the National Library of Medicine, a U.S.-Italian Collaboration published the first guidance on the scientific rationale for early ambulatory treatment of COVID-19 as the only hope to reduce the chances of hospitalization or death once COVID-19 is contracted [5].

These guidelines have been updated and adapted as shown in the Figure 2 and largely apply to adults over age 50 and those with medical comorbidities. The principles include using off target antiviral treatment (hydroxychloroquine, ivermectin, favipiravir, combined with an antibiotics [azithromycin, doxycycline] to provide synergism and coverage for bacterial super infection as soon as possible even before confirmatory testing is completed [6,7]. By day five or if any pulmonary symptoms develop, treatment of cytokine storm with corticosteroids is the next step [8]. Finally, given the disastrous risk of micro- and macro-thromboembolism with activation of thromboxane A2 and the development of antiphospholipid antibodies, full dose aspirin and intensification of treatment to include low-molecular weight heparin or novel oral anticoagulants is advised [9,10]. The shortest course of treatment with full resolution of symptoms is five days, average is 10 days, and for older individuals with multiple comorbidities or senior facility residents, a full 30 days of treatment is advised. The COVID-19 pandemic has called for superior discernment of an evolving yet imperfect universe of scientific information forged with clinical judgement and the art of medicine as the only immediate path to stem the tide of hospitalizations and death. The second pillar of pandemic response deserves the highest attention by public health officials and the U.S.-Italian treatment algorithm should be front and center in the COVID-19 global crisis [3].
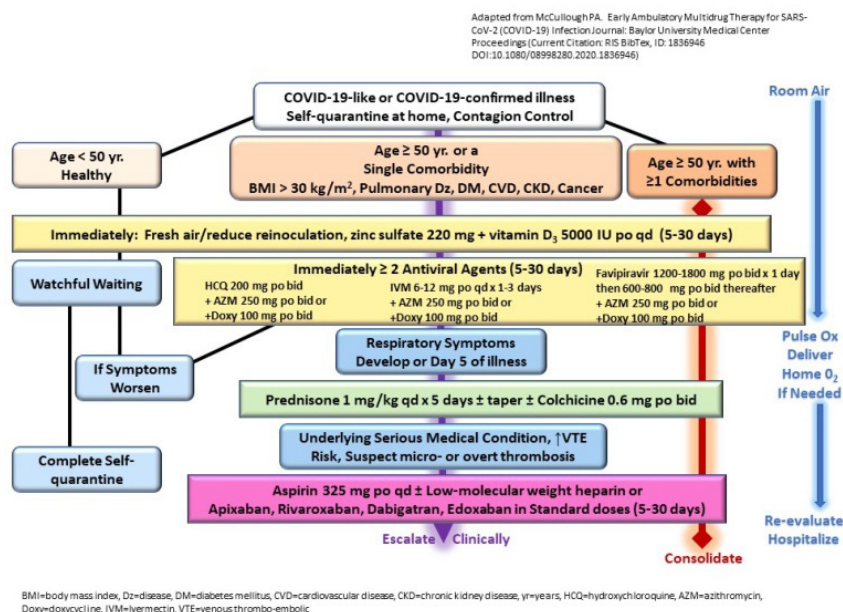
Figure 2. *Protocol treatment of early COVID-19 like and confirmed COVID-19 syndrome in patients at home or non-hospital facilities in self-quarantine. Yr: Year; BMI: Body Mass Index; Dz: Disease; DM: Diabetes Mellitus; CVD: Cardiovascular Disease; AZM: Azithromycin; Doxy: Doxycycline; HCQ: Hydroxychloroquine; IVM: Ivermectin; Mgt: Management; Ox: Oximetry*

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